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HERTZLER'S MONOGRAPHS ON SURGICAL PATHOLOGY

SURGICAL PATHOLOGY
OF THE
SKIN, FASCIA, MUSCLES,
TENDONS, BLOOD AND
LYMPH VESSELS

By

ARTHUR E. HERTZLER, M.D.

MONOGRAPHS ON
SURGICAL PATHOLOGY

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Professor of Surgery, University of Kansas

SURGICAL PATHOLOGY OF THE DISEASES OF BONES

SURGICAL PATHOLOGY OF THE SKIN, FASCIA, MUSCLES, TENDONS, BLOOD
AND LYMPH VESSELS

In Preparation

SURGICAL PATHOLOGY OF THE GENITO-URINARY ORGANS

SURGICAL PATHOLOGY OF THE FEMALE GENERATIVE ORGANS

SURGICAL PATHOLOGY OF THE GASTRO-INTESTINAL TRACT

SURGICAL PATHOLOGY OF THE PERITONEUM

Others to Follow

SURGICAL PATHOLOGY OF THE MAMMARY GLAND

SURGICAL PATHOLOGY OF THE DISEASES OF THE NECK

SURGICAL PATHOLOGY OF THE MOUTH AND JAW

SURGICAL PATHOLOGY OF THE THYROID GLAND

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260 Illustrations



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P R E F A C E

MORE patients present themselves in this clinic hopelessly sick with malignancies, the result of neglected or maltreated simple lesions of the skin, than from cancer of the uterus or mammary gland or the lip. These simple lesions of the skin adequately treated early would rid these patients of their disease. The fundamental difficulty seems to be that those who treat the simple lesions do not see the end result. When recurrences come either the patient recognizes the error made and wants no more of that particular doctor and seeks advice elsewhere, or they do not recognize the relation of their new complaints to the former lesion and set forth in new quests for relief. In either event the lesson is lost to the individual who first treated them.

It is the tiny lesions which are important. It requires no apology to treat them as serious menaces to the patient. It is not the marring of the hypothecated beauty of the patient but the ultimate danger to life of the patient that should appeal to the surgeon. Surgeon! It is to laugh! Yet it takes more clinical judgment to apply the proper treatment to these various little growths than it does to remove a goiter or a uterus.

I have not disdained therefore to consider the very beginning of these lesions. It is only by beginning here that one is enabled to understand their life history. To more clearly set forth the life history of some of these growths I have made certain realignments in classification. The patients with elevated lesions, commonly classified with the basal celled carcinomas, so often come with metastases after the wart has been treated by measures effective in flat basal celled lesions, that I have placed them in a separate group. Whether my theory of origin is correct is quite beside the point. The important thing is they often recur or are followed by metastasis when inadequately treated that there is no question of their clinical difference from the flat lesion.

The melanotic lesions also have received special attention. I have attempted to reclassify them to harmonize with clinical experience. I know the life history of these various lesions but I have not been able to present them in terms of histology satisfactory to myself but it may be hoped that even so much as here presented will stimulate others to a closer study of these very common lesions.

In discussing the genesis of thrombosis I have boldly set forth the results of my experimental study. I have done this because clinical experience has all too well emphasized the fundamental correctness of the conclusions arrived at in experimental work: never ligate a vein when in the state of reaction.

The purpose of the book is to present the result of observations in the clinic, or operating room with only incidental discussions of the findings of the laboratory. Pathologists will therefore please ignore the presentation of my own views. I have no quarrel either with them or with science; it is the art of medicine I seek to serve.

ARTHUR E. HERTZLER.

Halslead, Kansas
4-5-'31

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PART I

CHAPTER I

Ulcers of the Skin

ULCERS generally, in the minds of most clinicians, rank low as objects of surgical interest. However, they present so much of fundamental importance in surgical pathology that a somewhat detailed discussion of their basic factors may be presented without apology.

An ulcer may be defined as a loss of an area of the covering skin or mucous membrane which, at least temporarily, shows little tendency to heal. That is to say, a destruction of tissue is not an ulcer until a reaction has taken place in its base and about its border which prevents its healing, or that some local agent on the surface itself or some constitutional condition prevents the initiation of the process of healing.

It is necessary to distinguish between a superficial injury, a granulating surface, and an ulcer. Obviously a superficial wound which has not yet had time to declare its class should not be called an ulcer. A granulating surface which shows epithelial activity about its border indicating that healing is in progress is not an ulcer. An overproduction of granulations which delays the healing process in such cases but does not entirely prevent it is not an ulcer within the meaning of this chapter. The granulations may even be so exuberant that a real tumorous condition is produced which delays healing entirely for a time until such surplus granulations regress spontaneously or are destroyed by some chemical or mechanical measures. Such cases epithelialize as soon as the exuberant granulations are removed. The potentiality for healing is never entirely lost. Such granulations may continue so long, however, that changes in the tissues surrounding the ulcer become such that healing cannot take place even after the excessive granulations have been removed. In such the potentiality to heal is lost. On the other hand the reaction within the ulcer itself may be such as to prevent healing in the absence of any mechanical factors. The nature of the infection may be such as to pre-

vent positively the initiation of the processes which lead to healing. The nature of the infection may be known, as in the tuberculous ulcer, or unknown as in the phagedenic ulcer. All such cases require the services of the surgeon, or long periods of time, for the healing of the ulcer.

Why Ulcers Do Not Heal. Before considering the various types of ulcers, and the factors on which their existence depends, some fundamental conditions must be considered which are common in a general way to all ulcers. We disregard for the moment the question of their primary etiological factors and seek to determine why they do not heal. Why ulcers form is primarily the problem of the pathologist, but how they look and how to get rid of them concerns chiefly the surgeon.

In approaching this subject it is desirable to discuss first those factors common to all ulcers. Having done this it is of immediate surgical importance to consider certain clinical groups in order that fundamental conditions necessary for their cure may be established.

General Considerations. We will discuss here the anatomic factors of disturbed wound healing. In a healing wound the exudate coagulates on the surface of an ulcer producing a scab. Beneath this scab fibrin bundles form along which the newly developing epithelial cells extend. The development of these fibrin bundles is possible only when there is a point of attachment at some point toward the center of the ulcer. The scab furnishes this point of attachment. A scab is a layer of coagulated serum which covers the wound and is an essential to wound healing. Lacking the fibrin the new epithelium has no pathway across the ulcer and in consequence it piles up about the edges or lies dormant. Any factors which prevent the formation of a scab will prevent healing indefinitely. Even if a scab forms conditions beneath it may be such that fibrin bundles cannot form and in consequence healing is delayed. Such scabs are cast off time and again before healing begins. It is only when the conditions beneath the scab are such that fibrin can form that healing begins.

The optimal conditions for healing are provided when fibrin fibrils can form extending from the border of the ulcer to some site under the scab at some point toward the center of the ulcer. The epithelial cells travel along these fibrils and cover the surface of the ulcer. When this occurs and the fibrin fibrils become adult connective tissue the ulcer has healed.

When fibrin fibrils cannot be produced granular fibrin may be formed. In such cases the fibrin along which the epithelium spreads is produced by the fibroblasts. This is the common method of healing of infected wounds when a scab forms over them. The activity of the infection

may be so great that the protective forces must act until such a time as the toxicity of the bacterial products are reduced to such a degree that some sort of fibrin can be formed. In other words, it is healing by second intention. Any factors which prevent the formation of all fibrin stops the process of healing altogether. No fibrin, no healing.

Therefore it is only when factors are active in a wound which prevent fibrin formation and consequent epithelization that we are warranted in speaking of an ulcer. For a long time failure to heal may be due to bacterial action or other chemical factors alone before anatomic hindrance to healing develops. It becomes necessary therefore for the surgeon to determine whether the failure to heal is due to chemical or anatomical complications. The surgeon may sometimes simplify his problem of distinguishing whether the failure to heal is due to persistence of the infection by employing a therapeutic test. In pyocyanus infections, for instance, the use of acetic acid, in staphylococcal infections ammoniated mercury, in syphilitic ulcers potassium iodide, may destroy the agent which has prevented healing. When the factors which prevented the ulcer from healing are removed it heals with astonishing rapidity. He knows at once that it was the persistence of the infection that prevented the healing. These old therapeutic tests should not be overlooked even in this era of highly developed laboratory technic with minute bacteriological analyses and serological tests.

Unfortunately the factor which prevents healing cannot be discovered in all cases. In such cases a bacterial agent may be hypothecated and attempts at its annihilation made or the combative action of the tissue cells awaited. While the tissues are making this attempt at destroying the injurious agent changes in the vessel wall and the connective tissue about them may become so extensive that even when the primary causative factor has been destroyed healing cannot take place.

The defensive measures which the tissues institute consist in the bringing to the wound various cells which may be grouped under the term "phagocytic." When the phagocytic process is prolonged to the stage when endothelioid cells and fibroblasts appear in the base of the ulcer the vessel walls and connective tissue proliferate. There is a time in such ulcers when the causative infections cease to act and the anatomic factors become dominant. In such cases even when the infection is allayed the ulcer does not heal because of the anatomic changes that have taken place during the time the infection was being combated by the protective agents of the body.

It is necessary to examine the development of these secondary factors more in detail. The classical granule is made up of loops of capillary

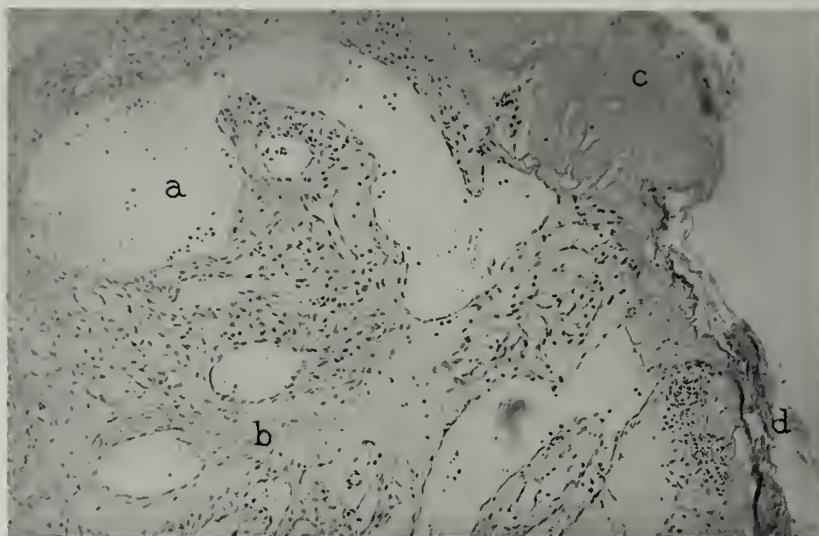


FIG. 1. Exuberant granulation tissue. This had remained unchanged for three months. *a*, Large blood spaces; *b*, connective tissue illy formed and poor in cells; *c*, epithelium piled up because it cannot cross the formless debris made up of granular fibrin and degenerated cells; (*d*) covering the surface.

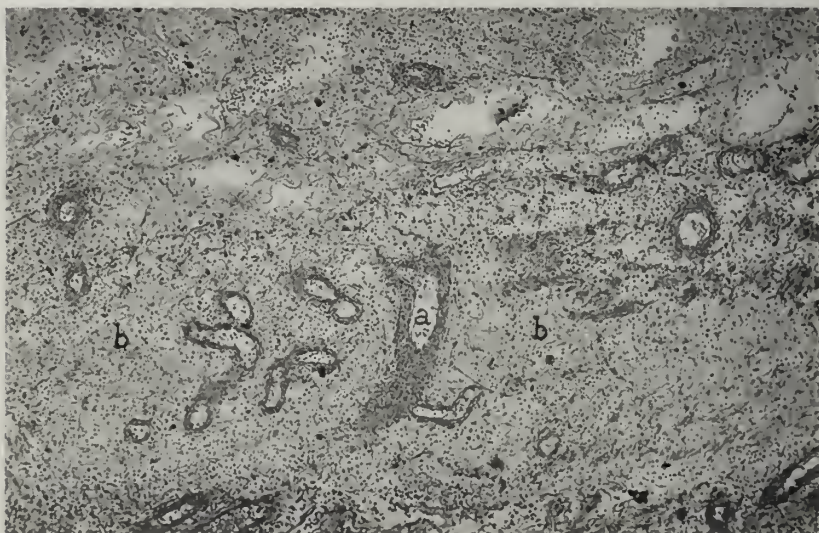


FIG. 2. Defective granulation tissue. This was removed from the border of a surgical infection which had remained unhealed 3 months. *a*, Vessel with thick wall infiltrated with round cells; *b*, illy formed connective tissue in the meshes of which are deeply staining round cells.

vessels surrounded by round cells, endothelial cells, and fibroblasts, as every sophomore learns, and sometimes remembers. The relation of these to types of cells need not be discussed here. When there is any disturbance in healing of normal granulation tissue it comes about either by unfavorable conditions in the connective tissue about the young vessels or in the walls of the vessels themselves. The rapidly developing granulation tissue, the "proud flesh" of the old authors, is made up of large blood spaces surrounded by round cells sparsely scattered in a

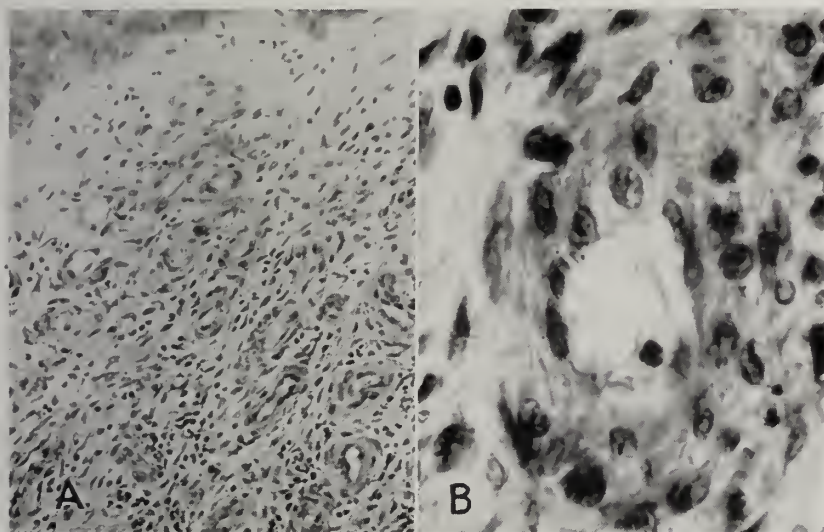


FIG. 3. Border of a chronic ulcer. *A*. Dense keloid-like fibrous tissue about the border and base of the ulcer. The vessels are numerous but thick walled being surrounded by the fibrous tissue. *B*. High power of an individual vessel. The vessel wall is made up of large endothelioid cells which all but occlude the lumen.

structureless exudate (Fig. 1). This exudate is incapable of coagulation, hence no fibrin can form on the surface of the granular area capable of organization. Such granules may remain unchanged for months. Usually the perivascular area becomes infiltrated with cells which may after a time lead to the formation of scar tissue. In such cases the vessels narrow and normal fibroblasts become more or less active (Fig. 2). These changes may take place very slowly, and may come to a standstill at any stage of the process. The familiar granuloma pyogenicum represents this state. In such cases the walls of the vessels may gradually thicken until they become incapable of supplying nutriment to the indolent healing process. If this process continues the vessels may become almost entirely obliterated (*A*, Fig. 3). The relation of blood vessels and connective

tissue varies. In the more slowly developing granules the connective tissue between the vessels may predominate (*B*, Fig. 3), and the ultimate result may be the formation of a fibrotic nodule. In this manner the ulcer may become surrounded by a keloid-like border. The connective tissue in such cases is made up of heavy bands which stain palely with acid dyes. The fibrous bands are interspersed with a few deeply staining spindleform nuclei.

When the vessel walls have become so thick that they are all but obliterated the ulcer becomes permanent because all nutriment is shut off, and healing will not begin until a new blood supply is provided. A classical example is seen in long continued ulcers of the leg.

In such cases it is obviously necessary to provide a new bed when skin grafting on old ulcers is contemplated. The older surgeons recognized the need of a new circulation but instead of excising the entire ulcer they made numerous cross incisions through the base of the ulcer which allowed the new vessels to reach the bed and thus start the healing processes anew.

The unfavorable conditions produced by the local changes in the vessels just detailed may be complicated by other factors, notably changes in the adjacent circulation as is commonly observed in varicose ulcers. Here the statics of the general venous circulation may produce stagnation that prevents healing. Other factors enter which are too numerous to discuss in the abstract since they may result from all sorts of local and general disturbances.

Granulation tissue does not form in all ulcers. In some cases no form of scab can form. The constant oozing of an irritating exudate keeps the surface of the ulcer moist. In such cases the base of the ulcer is made up of connective tissue native to the part which is infiltrated with leucocytes and other phagocytic cells. The whole may be overlaid with granular debris or a fluid exudate. The infection may have been so virulent as to prevent the formation of any sort of organized tissue and the ulcer remains in status quo indefinitely. This condition most commonly develops in those ulcers which result from deep infections which destroy the skin secondarily. Here healing is prevented by the continued action of the infection and only the annihilation of the organisms permits healing to begin. This type may finally heal after many months but the covering epithelium is likely to be irregular and the corium poorly developed and made up of dense fibrous tissue with thick vessel walls and more or less cell infiltration. Such healing is imperfect and after slight traumatism or unfavorable circulatory conditions the epidermis is prone to break down again and the ulcer reforms (Fig. 4).

The structure of abnormal granulation tissue has a further practical interest which may be mentioned in passing. Because the fields of round cells are traversed by thin-walled blood vessels a round celled sarcoma may be initiated. Only failure to determine the source of the tissue before a diagnosis is made could lead to such a grievous error. Nevertheless I once saw a jaw resected by a university professor because the professor of pathology had made the diagnosis of small round celled sarcoma from a section of a granuloma from an ulcer of the gum. No microscopic diagnosis should ever be made without a knowledge of the source of the tissue.

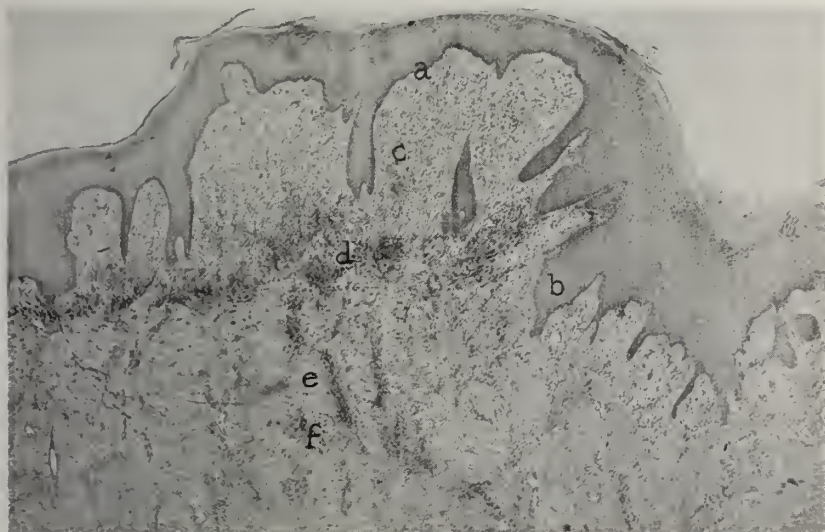


FIG. 4. Imperfect healing of a long existing ulcer: *a*, thin epidermal covering which dips more deeply at some points; *b*; *c*, beneath the epidermis is a layer of connective tissue in which, *d*, round cells persist indefinitely; *e*, small vessels with thick walls; *f*, heavy keloid-like bundles of fibrous tissue.

Special Considerations. Before entering into a discussion of the various clinical forms of ulcers it is necessary to consider some of the factors, special or more remote, which may be responsible for the persistence of the lesion. This is necessary because an ulcer may belong to one group at one time and change to another at a later date. For instance, a syphilitic ulcer of the leg may after many years take on the characteristics of a varicose ulcer, and may finally develop into a malignant lesion. That is to say, even the most specific of ulcers requires constant study lest it becomes something that it was not in the beginning. Obviously ulcers of unknown origin require a much more careful study.

It is necessary to understand the various stages an ulcer has undergone up to the time it comes under observation if we hope to apply the proper therapeutic measures. The factors here discussed are more or less arbitrary and it must be emphasized that two or more of them may be operative in a single case at the same time. Furthermore there may be



FIG. 5. Chronic ulcer in a scar. M., age 61. Leg burned 18 years ago. After many attempts at grafting, ulcerated area healed. Thirteen years ago an ulcer appeared which has gradually spread. Now it covers a triangular area 5 x 9 cm. The edge of the ulcer is firm, somewhat elevated. The base is covered with coarse deep red granulations.

factors not belonging in any of these categories, notably the various unfavorable constitutional states. One must not be so enamored of the ulcer that one forgets the patient.

I. The Nature of the Tissue in Which the Ulcer Occurs. Ulcers which occur in regions where the circulation is scanty and the subcutaneous tissue is abundant are apt to be persistent. An ulcer of the abdominal wall heals less readily than one on the face owing to the more

liberal blood supply in the latter region. Likewise in regions where the skin lies close upon hard tissue beneath healing may be interfered with. Ulcers in regions where the bone is superficial are notoriously resistant to treatment, for instance, over the tibia. Regions normally provided

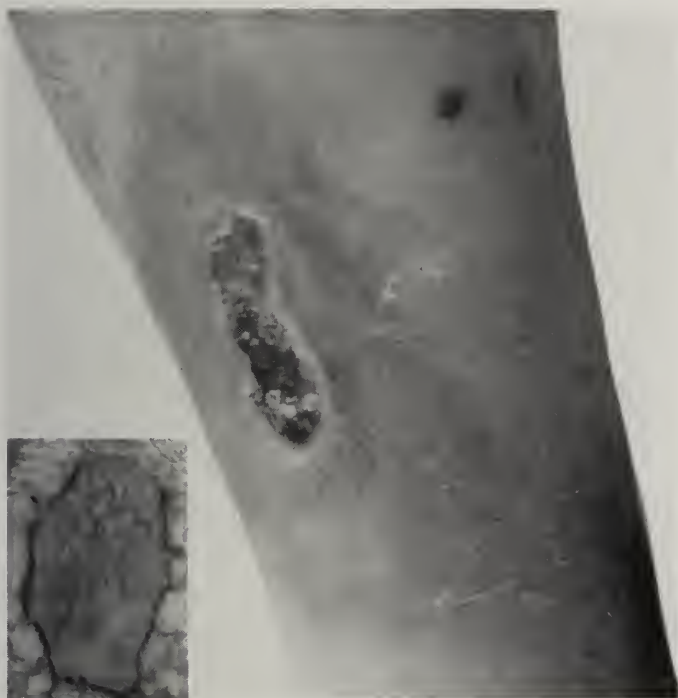


FIG. 6. Chronic ulcer of leg. M., age 42. Injured leg 5 years ago causing an abrasion. An ulcer formed which has continued since. Three years ago he sustained a fractured hip. Following the injury the leg was cold for a time but soon the circulation returned. No edema developed. The ulcer is shallow, 2 x 5 cm. in size, the base of which is covered with grayish granulations which discharge a serous fluid. The skin about the ulcer is deeply pigmented. Ulcer removed and base grafted. Failure. *Insert*, old varicose ulcer. The border is made up of a ridge of very dense fibrous tissue. The base likewise is scarred in which exquisitely sensitive papillations exist. Ulcer removed and the base grafted. Healing has been permanent.

with an abundant circulation may have the blood supply limited by disease or injury. Ulcers which form in scar tissue are familiar examples (Fig. 5).

2. **Anomalies of the Circulation.** Any marked disturbance in the circulation is a common factor in the causation and persistence of ulcers. The most familiar example is the venous congestion of the leg associated with the common varicose ulcer (Fig. 6). It is here, in fact, likewise the

chief causative factor. First of all there is an edema due to the imperfectly aerated blood in contact with the vessel walls making them more readily pervious to serum. The arterial and capillary circulation is influenced and undernourishment of the tissue follows. This results in an ineffective attempt to produce granulation tissue. Hyaline degeneration of the walls of the arteries complicates the situation which may proceed to an obliterating endarteritis. There results a granulation tissue the vessels of which have thick fibrous walls incapable of providing effective



FIG. 7. Trophic ulcers due to nerve lesions. *A*. Ulcer due to nerve injury. M., age 33. Injured leg in sawmill 18 years ago. Following this ulcers formed on ball of foot and heel. These have never healed. *B*. Ulcer due to occult spina bifida. M., age 14. Ulcers formed spontaneously and have never healed.

nutrition for healing. This vascular embarrassment is apt to be more pronounced in areas in which the tissue is sparse of vessels as that over the tibial crest, and for the same reason the associated infection is more apt to be intensive and add its burden to the healing process. While the foregoing remarks apply chiefly to the ubiquitous varicose ulcers of the leg they may become the dominant factor even in the specific ulcers, particularly tuberculosis and blastomycosis after the disease has existed for a long time.

3. **Disturbances of Innervation.** Any area in which the trophic nerve supply is destroyed is prone to ulcer formation which shows little

tendency to heal (Fig. 7). Loss of sensibility makes these regions more prone to injury, leading to the formation of an ulcer in the first place, and once formed, contributes to its persistence. On the other hand ulcers of any origin may by local changes so affect the nerve supply that they become secondarily trophic ulcers, at least in part.



FIG. 8. Pyogenic infection of the skin. M., age 40. Three weeks ago began with an itching pimple. Spread rapidly following violet ray treatment. Multiple superficial ulcers, soft indurated skin between ulcers. Wassermann negative. Healed in 10 days under ammoniated mercury ointment. The forms and situation might suggest syphilis.

4. **Local Irritation.** The irritation may be mechanical or chemical, or both. Delayed healing may result in an excessive secretion which becomes inspissated and the resulting crust may interfere mechanically with healing. The secretions from the original ulcer by coming in contact with previously unaffected skin may produce new ulcers (Fig. 8). Escape of contents of viscera may act as irritants, notably feces, urine and bile. Specific digestants such as saliva, gastroduodenal, and particularly pancreatic secretions, may not only contribute to the persistence of an ulcer but may of themselves cause them.

5. **Size and Form of the Ulcer.** Ulcers with vertical borders heal more readily than those with undermined borders. The latter are nearly always due to some process beginning beneath the skin and destroying it secondarily. This is more commonly noted in specific ulcers, such as in tuberculosis. The form of the border indicates an unfavorable base for healing and the overhanging edge must be eliminated before healing can



FIG. 9. X-ray burn of many years' duration. F., age 60. The overhanging border shows well on the right of the picture.

take place. The annihilation of the causative factor is, of course, a necessary concomitant, else the ulcer would immediately return. Excessive granulations may be protuberant, forming a ridge about the periphery of the ulcer, due to excessive epithelization, thus preventing its extension. Obviously, size in itself forms a serious barrier (Fig. 9). Even if epithelization does proceed in a normal manner at first, if the surface to be covered be great the bed of the ulcer may so change as to prevent complete recovery. This is seen in extensive burns. In such cases newly formed connective tissue in the base of the ulcer contracts the area to be covered by epithelium.

6. **Nature of the Base of the Ulcer.** The state of its base is a factor in healing. Exuberant granulations, the "proud flesh" of the old authors, by protruding above the surrounding epithelium may delay healing indefinitely (Fig. 10). Until this is destroyed epithelization is impossible.



FIG. 10. Exuberant granulation tissue in the base of an ulcer. M., age 36. Seven years ago leg was injured. Whole calf swelled and so remained when much on it, for several years. Three years ago sudden pain in leg and it swelled again. One year ago bruised leg and ulcer formed. Wide area of deep red, firm indurated skin in the center of which is an ulcer with slightly overhanging border. The base is coarsely granular of deep red color. Temporarily healed under bandaging and elevation.

Persistent infection prevents the formation of a granular base and healing is delayed. An ulcer with a fixed base does not heal rapidly because the factors which fix it destroy the circulation. Ulcerations which have become attached to a deep fascia or ulcers located in regions normally poor in circulation such as ulcers over the crest of the tibia are familiar examples.

7. **Hyperplasia of Epithelium About the Border of the Ulcer.** In some long standing ulcers in which, because of the nature of its base, the epithelium cannot cover it the epithelium spends its energy in local hyperplasia (Fig. 11). Even if the base changes so that epithelium could normally spread over the ulcer it is unable to do so because of the local proliferation. The epithelium sends long prolongations into the connective tissue beneath. This border may extend and a malignancy occurs



FIG. 11. Epithelial hyperplasia about an ulcer. M., age 42. Ulcer of many years' duration. The border of the ulcer is made up of hyperplastic keratotic epithelium. Prompt healing followed excision.

and cancers of the Marjolin's type result. The borderline between the benign and malignant is indefinite. In most cases even when histologically malignant they are not clinically malignant.

Such are some of the factors which involve the healing of ulcers. Therefore before the treatment of an ulcer is begun it is necessary to determine not only the agents which brought it into being, but also the factors which cause it to persist. The infection must be banished and a blood supply must be available to bring to the affected area a serum capable of forming fibrin. Irritating factors, mechanical or chemical, which prevent the formation of fibrin, must be eliminated. The funda-

mental factor, let it be repeated, is that local conditions must be so altered that an exudate is provided which is able to produce fibrin: no fibrin, no wound healing. The simple removal of irritating factors, bacterial produces, mechanical incrustations, intestinal ferments and the



FIG. 12. Ulcer following erythema induratum. F., age 35. Ulcers outer side of right calf which began as small piniples four months ago. The bases of the ulcers are covered with coarse reddish gray granulations, the borders slightly overhanging. Eight healthy children, three miscarriages. Wassermann negative. Refused to heal with ammoniated mercury and potassium iodide. Healed with wet dressings of calomel in limewater. *Inserts: A*, the cells of the ulcer destroy the epidermis from beneath; *B*, the cells are small round and polynuclear.

like, may be sufficient to allow this process to take place. Usually, however, it is necessary to correct the disturbance in the circulation by eliminating the venous congestion or by increasing the blood supply by excising the scar tissue about the ulcer and with it the sclerosed vessels. Excessive piling up of epithelium about the border of the ulcer calls for its removal.

Classification. After these preliminary remarks we may proceed to the consideration of the various types of ulcers which are of clinical interest:



FIG. 13. Ulcer following Vincent's angina. M., aged 14. Began 8 months ago with sore mouth and difficulty in swallowing. Lump behind jaw began to form several months ago. About 3 weeks ago an abscess broke into the mouth. Neck was poulticed and ulcer of skin formed. Mass under angle of jaw over which skin is destroyed. Uvula ulcerated away, posterior pharyngeal wall ulcerated and covered with gray moss. Both lungs dull, sounds diminished. Ovoid area of skin ulcerated by mass protruding from beneath. Deep reddish mass covered by gray exudate protrudes from base.

I. Nonspecific

1. Ulcers Due to Unknown Infections
2. Nutritional
3. Neurogenic
4. Painful Ulcers
5. X-ray Burns

6. Electric Burns

7. Staphylococcic

II. Specific

1. Tuberculosis
2. Syphilis
3. Blastomycosis

NONSPECIFIC ULCERS

Those ulcers which are caused by conditions other than demonstrable organisms are included under this head. Even the form recognized as

staphylococcic is included here because it is not capable of demonstration as a diagnostic measure because this organism can be cultured from almost any ulcer.

Ulcers Due to Unknown Infections. Under this caption may be included a number of ulcers of which we do not know the actual cause, even approximately. The circumstances under which they occur is more or less well established. Some of these begin beneath the skin and destroy it secondarily. I am including here erythema induratum, ulcers following Vincent's angina and some occurring in the terminal stages of



FIG. 14. Ulcer of the cheek in leukemia. M., age 9. Tonsillitis 3 weeks ago. Gangrene began 10 days ago. Healing advanced well but he had 160 thousand large mononuclear leucocytes.

acute leukemia. Not infrequently ulcers form following an injury which run the general course of erythema induratum but lack the preliminary lesion. Occasionally ulcers form in wounds operative and accidental, in which a low grade ulceration develops which persists indefinitely despite all treatment. They have the aggravating persistence and general appearance of phagedenic ulcers. Finally the self-inflicted ulcers of hysterics must be remembered. These are usually located in regions accessible to the favored hand.

It is a matter for encouragement that from time to time lesions are removed from this group and are placed in the specific group as the causative factors are discovered.

Pathogenesis. In some of these cases there is local reddening of the skin with edema. In others the skin is bluish with no other change

beyond the actual borders of the lesion. Pain is variable: sometimes it is spontaneous, sometimes there is only tenderness on pressure. Some are painless throughout, others only after scar formation has begun. Some are relatively acute in onset, others require months for their formation.



FIG. 15. Varicose ulcer of leg. F., age 65. For 30 years varicosities of lower medial surface of the leg. Ulcers have alternately healed and broken down again. Ulcer 3 x 5 cm. occupies the center. Many smaller ulcers perforate the hard thickened skin. Entire subcutaneous tissue of this region is firm, does not pit on pressure.

The termination is in harmony with the underlying disease. When they are complications of other disease their outcome depends on the primary lesion. Some are exceedingly chronic.

Pathology. Erythema induratum appears first as a red nodule protruding above the surface yet extending into the deeper tissues. After the ulcer forms the base is dull and coarsely granular with overhanging

border and hyperemic skin surrounding it. They are usually found on the legs (Fig. 12) but may be found on other parts of the body. Often they are multiple. They may be preceded by constitutional disturbances and present the general picture of erythema nodosum, from which they are not definitely separable. Ulcers following Vincent's angina present a necrotic base with overhanging reactionless edge (Fig. 13). While, of course, the causative agent of Vincent's angina is known the skin ulcers resulting therefrom may fail to reveal the spirillum and they must be



FIG. 16. Acute ulcer due to a thrombus in a vein. M., age 36. Since many years has had dilated veins on his calf. Recently an area of inflammation developed incapacitating him. An area of skin 2 x 3 cm. is defective. In the bottom are blood clots from which the recently covering vein walls have become eroded. Excision.

managed as those of unknown origin. The ulcer complicating acute leukemia (noma) is a necrosis of the cheek (Fig. 14). This lesion follows various constitutional diseases and is not specific for leukemia.

Histology. The erythematous ulcers show varying degrees of round and polynuclear cell activity in most cases (*Insert*, Fig. 12). Those associated with mouth lesions show little but massive death of tissue. Those ulcers which occur above the ankle in the later stages contain epithelioid cells after healing has begun but never definite tubercles nor giant cells.

Nutritional Ulcers. These are the commonest of ulcers and the most common cause is congestion due to interference with the return flow of blood as seen in varicose ulcers. Ulcers belonging to this group are seen

also in scarred areas following burns or other injuries (Fig. 5). The scar tissue limits the available nutrition. Any ulcer may come into this category when in the process of development or healing the vessels become obliterated by thickening of their walls or compression by fibrous tissue.

Pathogenesis. The disturbance of the venous circulation causes congestion in the areas they drain, most commonly seen in the lower medial



FIG. 17. Varicose ulcer of leg. F., age 65. For 30 years varicosities of lower medial surface of the leg. Ulcers have alternately healed and broken down again. Ulcer 3 x 5 cm. occupies the center. Many smaller ulcers perforate the hard thickened skin.

tibial region. Nutrition is disturbed which is manifested first by an intense deep bluish red color of the skin and finally by the loss of its surface (Fig. 15). The predilection for this region is probably due also to close contact between the skin and the tibia since ulcers are prone to follow slight injuries in the absence of obvious disturbance of the venous return.

Certain differences in the life histories of these ulcers depend on whether the deep or superficial vessels are at fault. In the former, following a thrombosis of the deeper vein, the result of injury or disease, the leg becomes edematous and an ulcer may form with or without reaction of the surrounding skin. In cases in which the deep thrombosis is due to local injury a double factor becomes operative.

In those cases of varicosity of the superficial veins ulcers may be produced by phlebitis followed by thrombus formation (Fig. 16). In such cases if the thrombus invades both the vessel wall and the skin, severe, even fatal, hemorrhage may be caused. If this accident does not occur scarring with chronic ulcer develops.

Frequently a chronic eczema exists for a long time before an ulcer forms. Maceration of the skin due to secretions retained by the bandage may cause secondary ulcers (Fig. 17). The scarring of the leg may involve the lymphatics so that a veritable elephantiasis is produced.

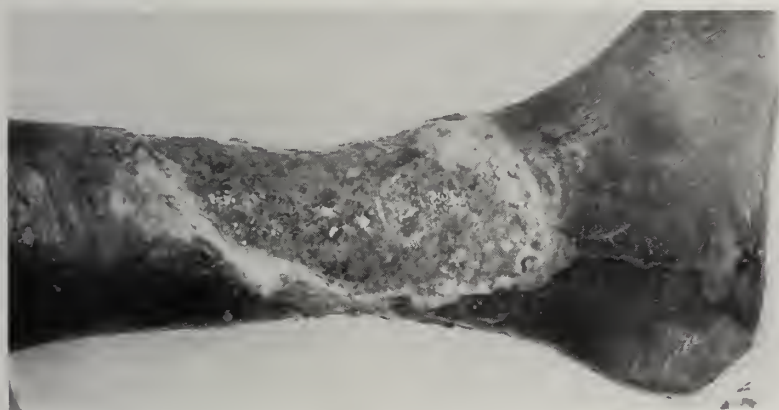


FIG. 18. Chronic ulcer of the leg. Duration of ulcer 25 years. Wassermann + plus. Ulcer not affected by any treatment. No epithelial proliferation.

Sooner or later the nerves become involved, presumably by their inclusion in the scar tissue of the ulcer, and pain is produced. It has been claimed that cutting of the nerve supply is followed by the healing of the ulcers. This is doubtful; the change may have been in the deep circulation.

Varicose ulcers may heal, with or without treatment, only to break down again. In patients long recumbent it is not unusual to see ulcers heal that had persisted for years. This gives rise to a peculiar belief among our forefathers, namely, if the ulcer would heal the patient would die. In patients long ill and confined to bed, as from cardiac disease, often the ulcer will heal. An old lady I once treated for decompensation watched her ulcer healing with consternation and she died, I believe, of fright as the healing process was about completed.

Pathology. In recent ulcers the borders may be sharp, even overhanging, fairly soft and surrounded by a wide area of inflammation. Dilated veins may lead to the ulcer, pass under it or to one side. In those

ulcers which are due to occlusion of the deep veins, no dilated veins may be visible. In these the ulcer has a more punched-out look and there is less likely to be an inflammatory halo. As time passes the attempt at healing produces definite scar formation with inclusion of the nerves and severe, even intense, pain may be produced. Small irregularities are seen about the border of the ulcer indicating a superabundance of connective tissue. Healing may occur in one segment of the ulcer, while extension takes place in another direction. Maceration and infection play perhaps a greater part in these than the lack of nutrition. In this way bizarre ulcers are formed resembling in a general way the contour of syphilitic ulcers. A positive

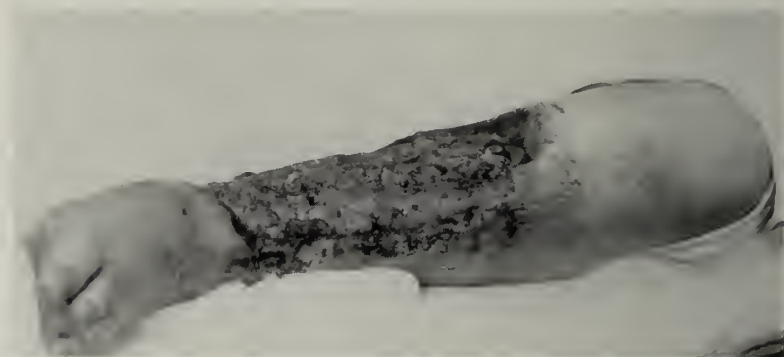


FIG. 19. Marjolin's ulcer. F., age 63. Began some 20 years ago with ulcer on the medial side of the calf. This gradually extended to present size. The border is firm, slightly overhanging in places. The base is mottled dirty gray and reddish. Section of border: epithelioma. Amputation refused.

Wassermann reaction may further complicate the diagnosis but it must still be remembered a syphilitic patient may have a varicose ulcer (Fig. 18).

The bed of the ulcer is covered with an uneven, intensely red, granulation tissue. There may be pronounced fibrous thickening in the base of the ulcer and this may extend under the adjacent skin with obvious thickening of the bordering epithelium.

The granulation tissue as well as the border of the ulcer may show signs of proliferation, conveying the impression of beginning malignancy. Just when such ulcers should be regarded as malignant is difficult to say. In the older literature cases are recorded in which the ulcer destroyed the underlying muscle and even invaded the bone. Occasionally after varicose ulcers exist for many years the border becomes prominent and more firm to the touch (Fig. 19). Sometimes pin-point epithelial cell nests can be made out by the naked eye or with a reading glass. These are called Marjolin's ulcer, but were first described by Home.

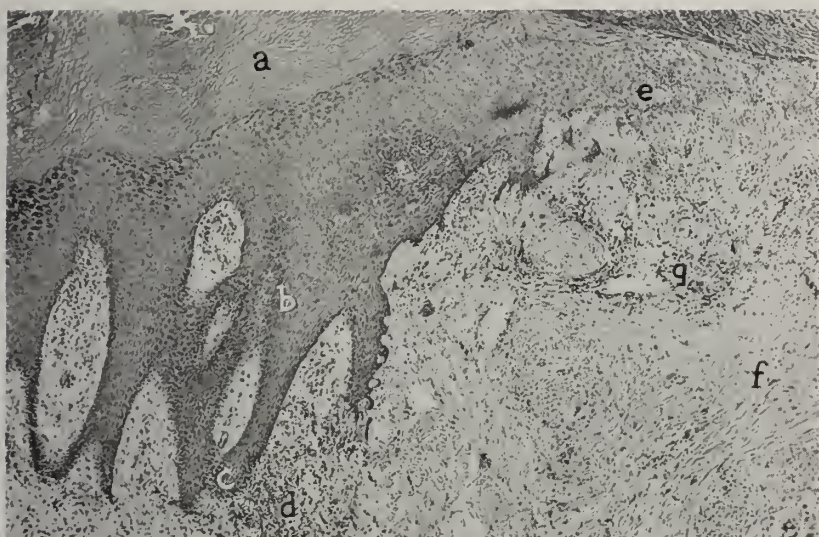


FIG. 20. Border of a varicose ulcer. This had remained unhealed many years. *a*. The corneal layer is much thickened; *b*, the granular layer is much thickened; *c*, about the terminal pegs there is round celled infiltration, *d*; *e*, the border between the epithelium and the connective tissue of the ulcer base; *f*, dense areas of connective tissue; *g*, round celled areas.

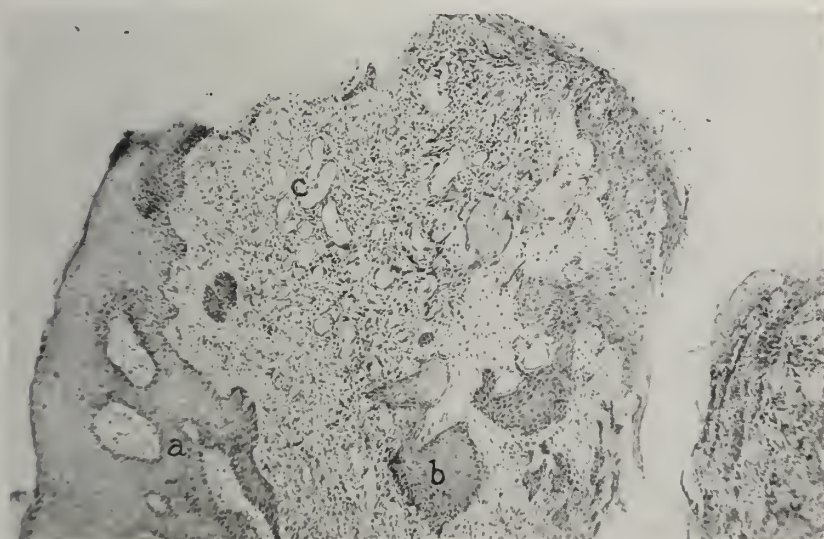


FIG. 21. Marjolin's ulcer of leg. F., age 63. Duration of ulcer 20 years. Edge of ulcer hard to touch. *a*, Hyperplastic epidermis; *b*, cell nests without notable change in cell type; *c*, large number of small vessels surrounded by dense fibrous tissue.

Histology. In the early ulcer the entire process is one of destruction. The epidermal edge terminates in dying cells (Fig. 20). The base of the ulcer is made up of granulation tissue of feeble reaction; the polynuclear and round cells are interspersed with stainless tissue. Later on reaction begins; the epithelium makes a feeble effort at repair. The granulation tissue consists largely of fibroblasts and more deeply staining acidophilic connective tissue. Granulation may exist for an indefinite time without change. So long as the vessels retain thin walls healing will take place if the normal circulation is provided. On the other hand the capillaries and large vessels may become thickened or compressed; hyaline degeneration follows and healing will not begin until the fibrous tissue is removed and a bed provided which can produce young granulation tissue.

The epithelium about the border may become thickened but there is no change in cell type. Malignant degeneration of chronic ulcers is not common. Old lupus ulcers are sometimes so complicated. There is an anatomic malignancy (Fig. 21) which is much more common than a clinical malignancy. The cells undergo changes in cell type and form nests but when these lesions are removed they do not return nor do they form metastases if untreated. The reason is plain to see. The increase of connective tissue at the floor of the ulcer (Fig. 20) which prevented its healing also prevents the spread of the developing epithelium locally and likewise the formation of metastases.

Neurogenic Ulcers. Ulcers resembling the preceding may be associated with a disturbance of the nerves supplying the skin in the affected region. One sees this in ulcers distal to the point of severance of nerves and in occult spina bifida and the like. Certain types of bed sores probably belong to this type. As to whether or not neurogenic ulcers occur without organic nerve lesions neurologists are not in accord.

Pathogenesis. Ulcers due to injuries of the nerves are of major interest to the surgeon. Following such an accident the skin becomes thinned, pale, obviously deprived of adequate nutrition. An ulcer develops and because of its poor blood supply refuses to heal. The ubiquitous bed sore following spinal injuries may be classed here.

In other lesions, like those associated with occult spina bifida (B, Fig. 7) and the more frequent perforating ulcer, the skin is not thinned—in fact frequently is thickened—and the demonstration of a nerve disturbance may be needed to establish its nature.

There is a type of ulcer regarding which neurologists seem to differ. It is the neurogenic ulcers of acute onset. Following a herpes-like lesion the skin and subcutaneous tissue break down forming a deep roundish or ovoid ulcer often extending into the fatty subcutaneous

layer, even to the fascia. It is difficult to exclude tampering on the part of the patient but I believe such suspected ulcers that do not heal under a plaster cast may strongly be suspected of being of true neurogenic origin.

I once saw a row of ulcers which developed along the course of the tenth intercostal nerve following an experience with a cyclone. The patient was not injured and was not a neurotic person and after a long time the ulcers healed.

Pathology. The vascular changes in ulcers of this type are not comparable to those of congestive or infective origin. There is little or no



FIG. 22. Painful ulcer of the malleolus. M., age 18. Pale, undernourished boy 8 months ago noticed bluish area over the left ankle joint. After a few months ulcers formed which have since persisted. The skin surrounding the ulcers is deep blue in color and soft to the touch and not painful. The border is undermined and elevated by a deep red, soft granulating mass.

attempt at repair. They may remain unchanged for years. The adjacent skin is deprived of nutrition so that even if the ulcer is excised healing is impossible. The border when cut across is dry, shining and grates under the knife.

Histology. Occasionally the bordering epidermis shows a feeble attempt to heal, but usually there is only a dense fibrous tissue containing but few elongated nuclei. The blood vessels are sparse, being obliterated for the most part by the proliferated connective tissue.

Painful Ulcers. These ulcers deserve special consideration because of their constant clinical characteristics and their uncertain causation. They are generally ascribed to circulatory disturbances.

Pathogenesis. They occur about the malleoli, usually just above the external. They begin as bluish spots which break down and produce characteristic ulcerations (Fig. 22). They resemble the ulcers which follow thrombosis of the deep veins but there is no sign of involvement of any of the veins, superficial or deep. The borders are usually undermined, which taken together with the bluish color of the surrounding skin, and in many cases obvious malnutrition of the patient, have caused them



FIG. 23. X-ray burn of the toes. M., age 42. Toes were X-rayed four years ago for ringworm. Ulceration of dorsum of tarsals and distal portion of the foot followed. The ulcerated area is indurated and in certain areas exceedingly sensitive to pressure. Amputation of toes. *Insert:* X-ray ulcer of the abdomen. Deep red firm granular surface is elevated above the surrounding reactionless skin.

to be regarded as tubercular. I have seen them mostly in undernourished young males. Recently Corlette has described them under the caption of painful ulcers and he cites a series of cases which healed promptly after the cutaneous nerves had been severed. It seems unlikely that they are neurogenic for they do not become painful until the borders have become infiltrated, usually after some months. In this also they parallel the ulcers following deep vein thrombosis. When treated expectantly they heal in from six to eighteen months.

Pathology. The overhanging borders are firm and elastic to the touch and are not sensitive to pressure. The base of the ulcer is formed by deep red fairly firm granulations.

Histology. The edges of the ulcer show mostly round celled infiltration; later endothelioid cells are numerous. The base is made up of granulation tissue in which the vessels remain thin-walled. There are no giant cells or other evidence of tuberculosis.

X-ray Burns. The too prolonged or improper use of the X-rays sometimes results in destruction of the skin which results in persistent ulcerations.

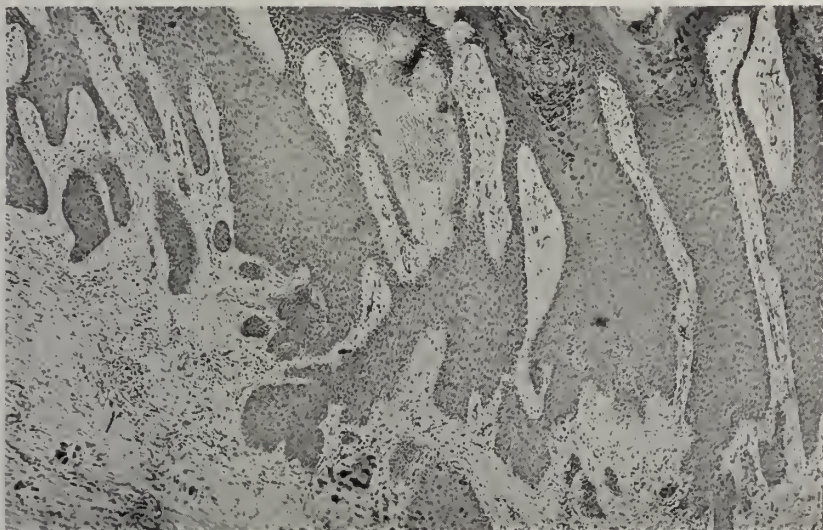


FIG. 24. Border of an ulcer due to an X-ray burn. F., age 66. Duration of ulcer 25 years. The epithelium is much hypertrophied, sending pegs deep into the corium, in some cases forming pseudo cell nests. Just beneath these is dense fibrous tissue with round celled infiltration.

Pathogenesis. The effect of the X-ray is to destroy the acidophilic character of the connective tissue of the skin. Usually weeks, often months, are required before an ulcer forms. The early lesions are irregular in outline, the surrounding skin hyperemic for considerable distances. The base is made up of dirty sluggish granulation tissue (Fig. 23). Later on the base is formed by a dense scar-like tissue over which the epithelium cannot spread and a permanent ulcer results (*Insert*, Fig. 23).

Pathology. Usually the history explains their origin. In the absence of this information the hyperemia caused by the presence of the abundant small vessels in the adjacent skin is suggestive. The border is firm, often giving a sense of elevation not evident on inspection. The base is firm, keloid-like. On section the density is confirmed by the resistance offered to the knife.

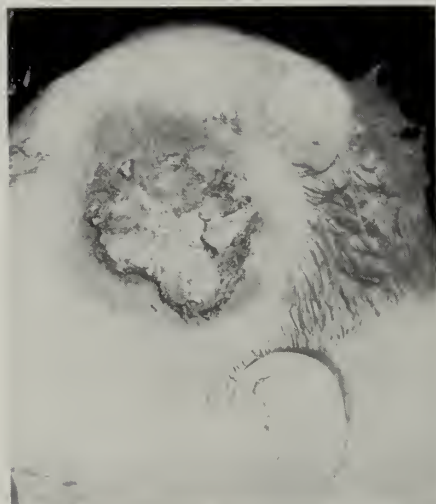


FIG. 25. Electric burn of the scalp. M., age 54. Injured by a live wire coming in contact with the parietal region. The border of the defect remained reactionless many months.

Histology. Early the change in the tinctorial reaction of the connective tissue together with some round cell infiltration is in evidence. Later the blood vessels about the border become dilated and the walls sclerotic. After the ulcer has attained its permanent form heavy bundles of fibrous tissue with round cells dominate the picture. About the border of the ulcer the epithelium commonly sends down columns of cells into



FIG. 26. Staphylococcic ulcers of the foot. F., age 19. Began as a small abrasion at base of one toe 4 months ago. Gradually spread to present size. Base of toes and lower metatarsal region covered with irregular superficial ulcers covered more or less with dirty grayish scabs. About the border of the affected area are a few small pustules. Healed in 10 days.

the connective tissue (Fig. 24). In late cases definite cell nests may form, suggesting the formation of epithelioma on the hands of the old time roentgenologists. In treatment burns the epithelial proliferation does not extend beyond the formation of harmless cell nests.

Electric Burns. Burns due to contact with electric wires produce lesions radically different from those due to the excessive use of the X-rays.



FIG. 27. Staphylococcic ulcer of foot. M., age 22. Chicken picker. Small papules formed 4 months ago on both feet. These soon formed ulcers. Sharply defined ulcers extending through entire thickness of skin. Surrounding skin but little reddened and indurated. Prompt recovery under ammoniated mercury ointment.

Pathogenesis. Usually contact with the current produces a white eschar of a considerable area of skin. The course is exceedingly prolonged because the circulation is destroyed for considerable distances beyond the visible lesion (Fig. 25). Many months are required for a line of demarcation to be established. This is longer in proportion as the deeper tissues are destroyed.

Pathology. The injured area is more or less circumscribed, depending on the extent of the injury. The skin is attached to the underlying tissue, not by proliferation but by fusion; welding would be a better word. This impression is emphasized on cross section.

Histology. The single specimen at my disposal showed a reactionless stainless tissue.

Staphylococcic Ulcers. Possibly these rather common ulcers should be discussed under the specific lesions. However, the ulcers contain such an abundant flora that the specificity cannot be demonstrated.

Pathogenesis. Usually without obvious injury ulcers quickly form. They begin as punctiform crater-like lesions which rapidly enlarge to the size they maintain. They persist with astonishing tenacity. They are

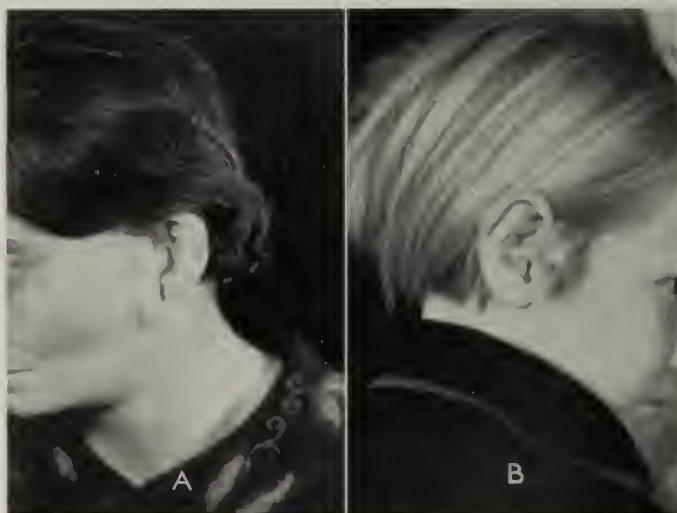


FIG. 28. Tubercular lymphadenitis. A. F., age 30. Enlarged cervical lymph glands, and a fluctuating tumor the size of a hickory nut in front of ear. Skin covering it is red. Conservative treatment. B. F., age 6. Abscess in front of ear; opened up, packed, recovered.

recognized by the rapidity with which they heal when ammoniated mercury is applied.

Pathology. The ulcers are irregularly ovoid with a soft overhanging border and a dirty grayish base. When these are confluent an ulcerous lesion with a serrated border may be produced (Fig. 26). Sometimes they form discrete lesions spread over wide areas (Fig. 27). Granulation tissue formation is not in evidence.

Histology. Histological material has not been available. Culture shows a variety of bacteria.

ULCERS OF SPECIFIC ORIGIN

There are a number of ulcers due to a specific cause that require separate descriptions. Those of interest to the surgeon are tuberculosis,

syphilis and blastomycosis. In the nonspecific ulcers the chief concern is the discovery and elimination of factors, circulatory and otherwise, which prevent healing. In the specific ulcers, on the other hand, the identification of the cause and its annihilation are the essential factors. In long standing specific ulcers the nutrition, innervation, etc., play a minor rôle in preventing recovery after the specific cause has been removed.



FIG. 29. Tuberculous ulcers of the neck. M., age 9. Two years ago following pneumonia had middle ear infection. Multiple abscesses appeared in the neck. These were opened but have never healed. Numerous superficial ulcers with soft bluish overhanging borders. The bases of the ulcers are deep red covered with a dirty gray exudate.

Tuberculous Ulcers of the Skin. Skin tuberculosis, including lupus, often concerns the general surgeon. This is readily understood when it is remembered that Duhring diagnosed as scrofuloderma the case Gilchrist later proved to be blastomycosis, the first case on record. Even more important is the fact that now, since the sporotrichal diseases are recognized, tuberculous skin diseases are often overlooked. This is true certainly in regions of the United States where all forms of tuberculosis are relatively rare. No case of lupus has been observed in this clinic. Cases

formerly regarded as tubercular are now recognized as blastomycosis. Indeed, few practitioners, among the surgeons, at least, are expert enough to make the diagnosis without the aid of the microscope. Albeit the rate of development should give a clue.

Tuberculous lesions may be found anywhere on the body, most commonly on the face in front of the ear, along the border of the sternomastoid muscle, and about the anus. While most commonly seen in persons afflicted with tuberculosis elsewhere they may be found even in otherwise healthy individuals.



FIG. 30. Gumma of knee. F., age 47. Swelling at outer side of knee began 9 months ago. Swelling and tenderness have gradually increased. Nodule size walnut, surface red, semifluctuating. Wassermann \pm plus. *Insert:* The patient urgently desired the removal of the tumor. The cross-section shows a reddish border enclosing a sharply defined, caseated area. Rapid recovery under mixed treatment.

Pathogenesis. In some cases ulcers result from suppurating glands. They are most common in the parotid region (Fig. 28), and over the sternomastoid muscle in under-nourished children. These are due to infection of the lymph glands, likely through the tonsils. Those ulcers which develop in front of the ear are possibly also derived from the glands.

In other parts of the body the lesion begins as a localized infiltration, bluish in color. After they attain a diameter of 1 cm. or more, the surface breaks down leaving an ulcer. Extension into the surrounding tissue may take place. The chief characteristics of tubercular ulcers are their great chronicity, though they tend ultimately to heal.

Pathology. The tubercular ulcer is characterized first of all by the soft overhanging border (Fig. 29). Even old ulcers maintain this character in which they differ from malignant ulcers. The trained touch knows. The bases of the ulcer are covered by a dirty gray debris generally less

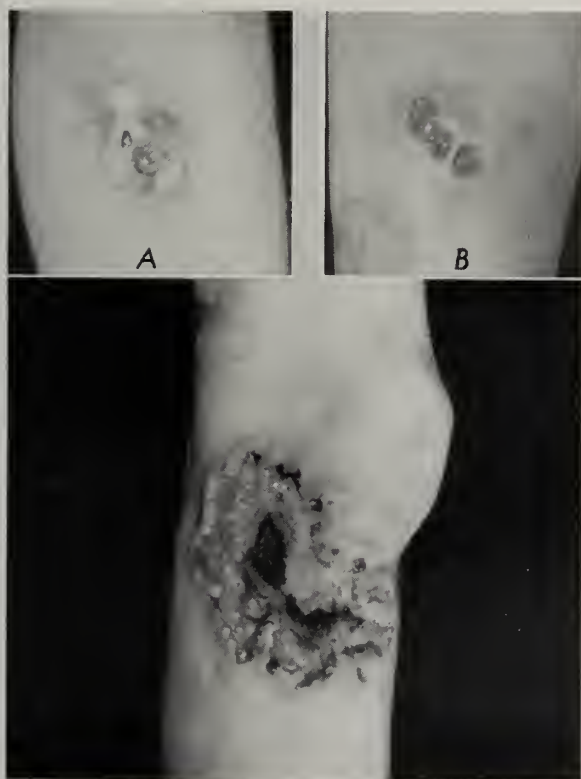


FIG. 31. Syphilitic ulcer of the knee. M., age 37. A year ago injured skin just below the outer surface of the knee. This healed but in two months ulcers began to form and extended to present dimensions. Now the ulcer is as large as the palm of the hand with irregular ovoid serrations about the border. The base of the ulcer is irregular; in some areas large pale granulations, in others soft half-necrotic masses protrude. Wassermann 4 plus. Healed in 4 weeks on mixed treatment. *Inserts:* A, partly healed ulcers; B, more active ulcers in a young girl. Form and arrangement of the ulcers is typical.

specifically granular than in nutritional ulcers. They are less likely to bleed on manipulation than malignant ulcers. Sometimes individual tubercles can be made out on the border by pressing out the blood under a glass slide. The tubercles appear as brownish specks in the lighter background of the anemic skin. Enlarged lymph glands may be found in the neighborhood. These may be due to secondary infection with pus

microbes or they may be tubercular and antedate the development of the ulcer. Lymph glands are seldom infected secondarily from the ulcer with tubercle bacilli. The skin surrounding a tubercular ulcer is usually bluish, or even a livid blue, which must be regarded as one of the most distinctive features of this type of ulcer.

Histology. The elemental lesion is of course the tubercle. The giant cells with their peripheral nuclei and necrotic protoplasm surrounded by small, round and epithelioid cells are unmistakable. Often, of course, the



FIG. 32. Blastomycosis. F., age 74. Began as small inflamed area 10 months ago. Coarse granular lesion covering greater part of the dorsum of the hand and bases of the fingers. Whitish areas are intermingled with reddish nodules. Healed under X-ray and potassium iodide.

lesion is not so plainly marked but typical giant cells and necrotic areas are usually demonstrable. It may be noted here that in necrotic areas in tuberculosis the nuclei disappear along with the other structures. In syphilis the nuclei remain relatively intact though the protoplasm of the cells be destroyed.

Syphilitic Ulcers. Only the ulcers of tertiary syphilis will be considered here. One of the most interesting facts in pathology is the predilection of the syphilitic ulcers for certain regions. The reason for this is a mystery. The regions in order of frequency are the lateral surfaces of the calf particularly just below the knee joint, the forehead, the region of the clavicle, and the back.

Pathogenesis. Usually the lesions are fully formed when they come under the observation of the surgeon. I have seen a number develop from the beginning. They begin as indurated, slightly painful areas (Fig. 30). The pain is seldom severe unless the lesion lies over a bone as

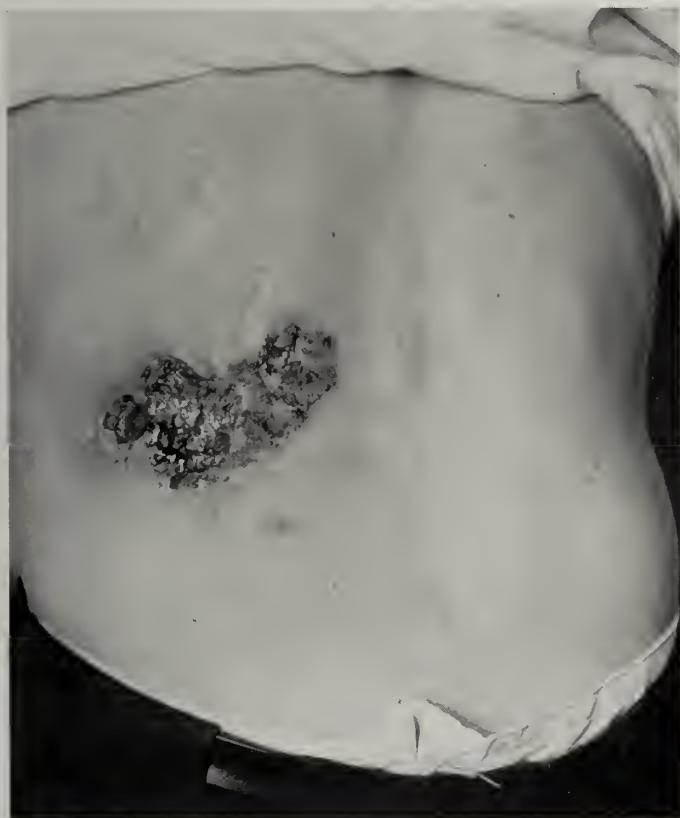


FIG. 33. Blastomycosis. M., age 31. Began 19 years ago as a small nodule. Gradually enlarged. Sometimes improved for a time under large doses of potassium iodide. An elevated ulcer the size of the palm of the hand. The border is firm and multiple papillary projections are seen along this line. The ulcer for the most part is covered with coarse granules, somewhat firm to the touch, which do not bleed readily. The area was resected and the denuded part covered with skin grafts. Free from recurrence seven years.

the skull, clavicle, tibia, etc., in which case the pain may be severe due to associated periostitis. Soon the surface becomes reddened and somewhat elevated. After ulceration occurs the pain lessens or ceases. To the primary lesions others nearby are added as separate lesions or at the margin becoming by their coalescence a large serrated ulcer. As the ulcers become older healing may take place in some areas while new

areas become affected. In this way wide areas are gradually involved such as the whole face, large areas of the back or leg. I have seen cases in which this sequence has continued for more than 20 years or until a proper diagnosis is made and adequate treatment applied.

Pathology. The gummatous lesion when completely excised and hardened shows a red and indurated border not sharply separated from the surrounding normal tissue (Fig. 31). In the center is a sharply de-

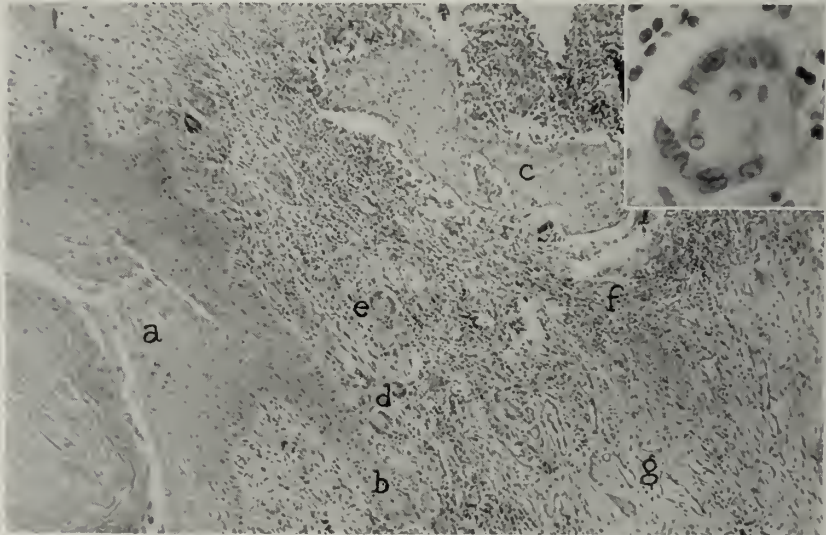


FIG. 34. Blastomycosis: *a*, hyperplasia of the epidermal epithelium with, *b*, deep prolongations of the papilla; *c*, with isolated cell nests; *d*, giant cells; *e*, some with the nuclei situated about the border of the cell; *f*, round cell infiltration; *g*, blood vessels surrounded by dense fibrous tissue. *Insert*, enlarged giant cell with specific organism.

finer caseated region (*Insert*, Fig. 30). Being spheroidal the skin becomes destroyed only at that segment of the sphere in contact with the skin. When the gumma softens the diameter of the cavity is greater than the area of skin destroyed. The result is that the recent ulcer has overhanging borders. The gumma is white, even pearly white in color. The color of the surrounding skin is red or deep red, less deep red or bluish than the tubercular ulcer. As the ulcer becomes older the skin whitens and assumes the color of the surrounding skin. The edge of the ulcer remains soft to the touch and the cavity is livid with soft, fragile, dirty, granulation tissue. This fragile base remains irrespective of the age of the ulcer but it does not bleed. In the long existing ulcers scar formation begins about the periphery and they may heal in one region while extending in

another. Healed areas may mark their presence by a long continued brown pigmentation.

The chief characteristic of the established syphilitic ulcers is their bean or kidney shape (Fig. 30). This is true of the individual lesion as well as of the grouping of several lesions and even of the remaining scars. This is one of the soundest signs in clinical medicine and is more dependable than the Wassermann reaction.

The shape of the lesion, the relatively rapid onset and the soft overhanging border make it easily distinguishable from tuberculosis and cancer with which it is commonly confused.

Histology. There are two things characteristic of syphilitic lesions. The first is the associated endarteritis and the second, that in broken down gummatous lesions the nucleus retains its stainability long after the surrounding connective tissue and the cell protoplasm has become degenerated. There are, of course, the spirochetes demonstrable by special stains.

Blastomycosis (Oidiomycosis-Ricketts). The skin becomes the seat of infection by a yeast fungus, the blastomyces. Here we need to be concerned only with the localized form though it must be remembered that the local lesion may be secondary to a generalized lesion.

Pathogenesis. The lesion begins as a vesicle, more commonly a pustule, which gradually invades the surrounding skin. The lesions vary from 1 to 20 cm. in diameter and may spread to much larger areas. They tend to heal in the center, in some cases forming a scar which is at first thick but which may become thinned or wrinkled as time goes on. The same is true whether the healing is due to the therapeutic measures or occurs spontaneously. When the lesion is in the neighborhood of a joint movements may be interfered with. In large lesions where the skin is wholly destroyed spontaneous healing cannot take place. The lesions may require only a few weeks to develop but usually some months are required.

Pathology. In the early stages the lesion is a small crater-like pustule. As the lesion spreads a number of centers of infection may cause the lesion to look like a modified carbuncle. Small pustules may be seen in the epidermis with the naked eye. When the granulation tissues form it is of a deep red "apple butter" color. The surface is irregular, papilliform (Fig. 32), firmer to the touch than ordinary granulation tissue. The lesion is fixed to the fascia and may even extend to the muscles. Usually the lesion extends papilla-like above the surrounding skin but in old lesions the affected area may be even lower than the healthy surroundings (Fig. 33). Such old cases may resemble syphilitic lesions very closely.

Histology. Within these abscesses are polynuclear and other cells and with them the specific cause of the disease—the blastomyces (*Insert*, Fig. 34). These are round, doubly refracting bodies several times the diameter of a red blood cell. Granules may be visible in the protoplasm of these structures. Eosinophile cells are sometimes present in great abundance. Giant cells resembling tubercular giant cells are frequently observed (Fig. 34). The surface epithelium may be destroyed leaving only the epithelial nests beneath the surface apparently unconnected with the epidermis. The resemblance to epithelial malignancy may be very close.

There is a marked prolongation of the epithelium downward. This may extend even to the underlying muscle. In old cases the resemblance to carcinomas may be close but there is less cell differentiation in most cases. Within these cell columns, or surrounded by them, are small abscesses.

Literature

The literature of ulcers is astonishingly vast, particularly in the earlier periods. It is obvious from the perusal of it that a variety of lesions were classed under this head which were due to specific causes. Conspicuous among these were the fistulous ulcers secondary to neglected osteomyelitis. Ulcerating bone tumors were included and those arising from irritated warts with metastases in Scarpa's triangle were clearly melanotic tumors (Pollock, St. George's Hosp. Rep., Lond., 1879, ix, 336).

It is scarcely necessary to go back earlier than Marjolin. His paper was first published in 1810 and repeated with additions in 1846 (*Dictionnaire de médecine*, ed. 2, Paris, 1846, xxx, 10). This attempts to classify ulcers and calls attention to certain fungating lesions which he believed to be malignant. From that time ulcerations which terminated in malignancy have been called Marjolin's ulcers. Sir Everard Home (*Treatment of Ulcers on the Legs*, Bulmer & Co., London, Ed. 2, 1801) in a monograph described a variety of ulcers, some of which destroyed the soft parts to the bone. The first apparently to confine his descriptions of ulcers which have gone malignant in the modern sense apparently was Caesar Hawkins in 1835 (quoted by Stapleton, *Dublin Med. Press*, 1851, xxv, 81). This old literature makes exceedingly fascinating reading but its perusal is without practical benefit because of the inclusion of all lesions apparently which produced loss of the skin.

White and Weidman (*Jour. A. M. A.*, 1927, 88, 1959) have called attention to the very obvious fact that many of the so-called malignant ulcers are nothing more than epithelial hyperplasias and are clinically benign. Cases in the literature in which recurrences occurred after operation, even after amputation (Woolsey, *Ann. Surg.*, 1906, xliii, 610). Cone (*J. H. Hosp. Bull.*, 1897, viii, 146) discusses malignancies developing on old sinuses in old cases of osteomyelitis.

The most extensive general discussion of ulcers in all their phases from the modern viewpoint is contained in Winiwarter's monograph on surgical diseases of the skin (*Deutsche Chir.*, Lief. 23, Enke, Stuttgart, 1892).

Painful Ulcers: Corlette (*Surg., Gynec. and Obst.*, 1929, 48, 811) has recently demonstrated that cutting of the nerve supply in painful ulcers of the malleolus is followed by the healing of the ulcers.

Blastomycosis: Ricketts (*J. Med. Research*, 1901, 6, 374). Gilchrist and Stokes (*J. Exper. Med.*, 1898, 3, 53) described the first case of blastomycosis on record, correctly diagnosing the case diagnosed as scrofuloderma by Duhring.

CHAPTER II

Benign Epithelial Skin Tumors

THE non-malignant tumors of the skin present a more or less heterogeneous group. They may be divided into three general classes; the papillomas, the adenomas and the cysts. The papillomas range in clinical importance from the perfectly innocent juvenile wart to the senile wart already the site of incipient malignancy. The cysts are usually classed into congenital, retention and inclusion. These are identical in structure and clinical significance. They rarely become malignant. Adenomas are accounted rare tumors by most authors but when all warts are sectioned they are encountered with astonishing frequency. They are frequently the starting point for malignancies.

EPITHELIAL PAPILLOMAS OF THE SKIN

The term "papilloma" is expressive of external form only and is commonly applied to any small tumor protruding from the surface. The term is applied to masses protruding from mucous surfaces as well as from the skin, and when so located are properly designated mucous papillomas. These will be considered in the chapters on diseases of the respective mucous surfaces.

As applied to skin lesions the term "papilloma" is too often applied indifferently to protuberant tumors irrespective of their anatomic structure. Small, soft masses, chiefly fibrous in structure, are sometimes called warts but are more properly considered under fibromas of the skin. The nevoid papillomas, so-called because of the peculiar cells at their base, are properly described with the melanomas whether they contain melanin-bearing cells or not. No matter what the epithelial covering may be all tumors harboring nevoid cells, whether pigmented or not, should be classed as melanotic for when they become malignant it is nearly always the nevoid cells that start the trouble.

The term "epithelial papillomas" therefore seems necessary to distinguish these tumors from other protruberant skin tumors. Even this term is only in a measure descriptive of them for in some the connective tissue participates in the formation of the tumor. However, it is the thickening of the epithelium, notably the cornified layer, that ultimately gives character and bulk to the tumor. When malignant tendencies ensue, and this is the important factor to the surgeon, it is the epithelial element

that becomes dominant. Many of these in the course of years gradually develop into malignant tumors. We designate them when in the transition period as "precancerous." This term expresses our ignorance as to whether or not they have become malignant. It expresses furthermore our collected experiences that such lesions commonly reach a stage when they are unquestionably malignant. It is this tendency for these tumors to become malignant that gives them dignity in the eyes of the surgeon. Otherwise their management might be delegated to cosmeticians. Surgeons have been too prone to neglect these growths. Therefore they will receive detailed consideration in this presentation.

Though generally benign, epithelial papillomas take a considerable toll of human life if neglected or maltreated. The various forms therefore should all be considered precancerous. This applies both to their undoubtedly innocent stage and the uncertain precancerous stage as well as the certainly malignant stage to be considered in the next chapter. Here is one group of tumors in which fatalities would be entirely prevented if they were considered more seriously.

There is no generally accepted classification for epithelial papillomas. However, epithelial papillomas are surgical lesions and an attempt will be made here to subdivide them in a manner best suited for the needs of the surgical clinic.

Two factors always come into question: whether or not they were congenital and whether they are circumscribed or diffuse.

Congenital Papillomas. Most congenital warts are melanotic in character and will be discussed in a subsequent chapter. Some with keratotic surfaces contain embryonal cells at their bases, consequently they also are classed with the melanotic group. Few epithelial papillomas are present at birth. Those that appear earliest in life are usually associated with excessive development of blood vessels. They occur most commonly on the temples. The linear type is most commonly situated on the trunk, often running parallel with an intercostal nerve.

Pathogenesis. These tumors are seen soon after birth and develop as the child develops. In rare instances they become malignant in early life and it is then the undifferentiated cells at the base which show activity. Late in life malignant tendencies are not unusual and then the growth is confined to the more mature epithelial cells.

Pathology. The surface is irregular in outline and feels rasp-like (Fig. 35). The increased vascularity may be apparent about their base. This disappears on pressure. These tumors are sometimes called angio-keratoma. When malignancy begins the surface becomes more nodular

and infiltration about the base may be noted. The non-vascular type is less elevated (Fig. 36) and their size is uninfluenced by pressure. The nodules are softer, depending on the thickness of the epithelial covering, and the entire lesion is more freely movable.

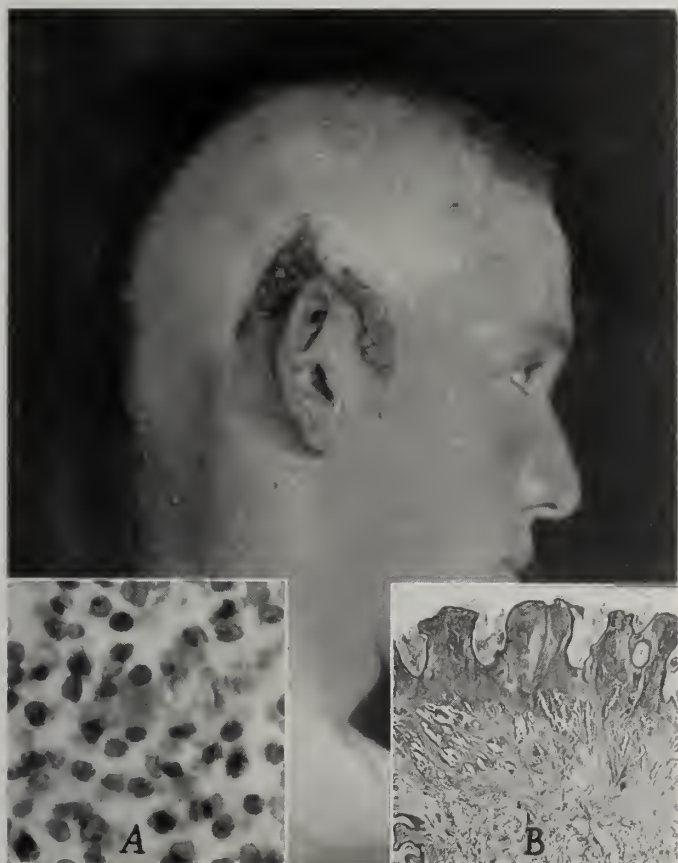


FIG. 35. Angiokeratoma of temple region. M., age 16. Rough warty spot above ear since birth. Lately has been forming crusts which cause bleeding when removed. Removed. Well 10 years. *A. Insert* shows cellular areas which lie between the numerous large vessels which lie below the keratinized epithelium. *B. Insert*, the vessels in the base of the tumor are numerous and large. Surrounding them are abundant round cells, the epithelium but little thickened.

Histology. Aside from the very obvious epithelial hypertrophy there is an abundance of vessels (*Insert B*, Fig. 35). The cells between the vessels are numerous and somewhat forbidding in appearance but rarely give rise to malignancies (*Insert A*, Fig. 35).

In the quiescent state there is a moderate thickening of the epithelium with an increase of fat glands (*Insert A*, Fig. 36). When the epithelium proliferates a very mild approach to malignancy is produced (*Insert B*, Fig. 36).



FIG. 36. Congenital papilloma developing malignancy. M., age 65. Birthmark above right ear. Upper end began to break down 6 months ago. The tumor is dense, papillary, file-like, moves freely with the skin. *Insert A* shows the structure of the lower part made up of cornified epithelium, fat glands and connective tissue. *Insert B*. The surface epithelium is much thickened but there is no direct invasion.

Juvenile Warts. These small tumors, common concomitants of budding young males, seem to have for their purpose the reminding him that of the sexes he is the inferior. They are ephemeral and are of cosmetic rather than clinical importance. Being of cosmetic importance they may

foster an inferiority complex which may be as important to the patient as the inception of cellular proliferation.

Pathogenesis. They seem to spring up full-grown without obvious beginning and disappear quite as mysteriously. It is reported that they have been transplanted which has led to the conclusion that they are infectious in character. It is only when such warts develop in regions where their mechanical presence causes trouble that they are of clinical importance. For instance, when on the palmar surface of the fingers or about the borders of the nails irritation may cause them to become painful.

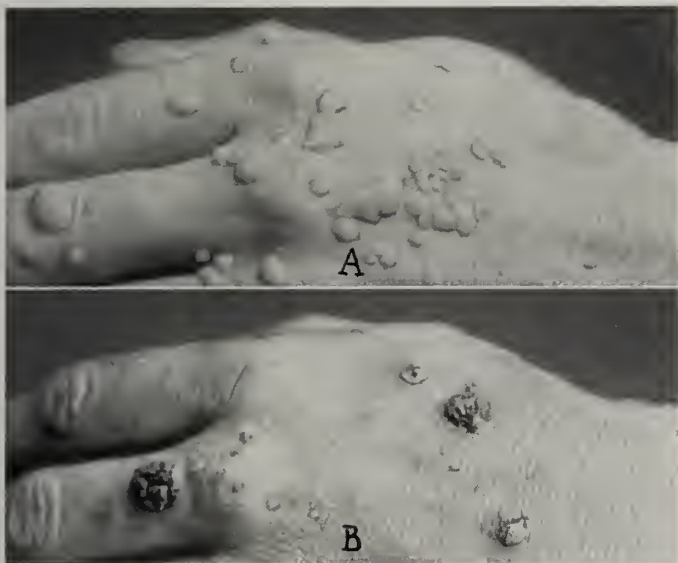


FIG. 37. Juvenile warts. *A*. Smooth papillomas in a boy of 9 years. *B*. Fissured warts in a boy of 12.

Pathology. These growths protrude as small smooth surfaced elevations (*A*, Fig. 37). Less commonly they are fissured (*B*, Fig. 37). They move freely with the skin. They show no changes in vascular arrangement. They appear as though set into the skin like the setting of a ring. When cut across this impression is confirmed. The wart appears as a dense pearly white structure.

Histology. The tumor is made up of epithelial hyperplasia situated on proliferated vascular papillae. There is usually a line of cleavage between the epithelium of the wart and the surrounding epidermis. The blood vessels show some increase in size but there are no foreign cells about the base.

Plantar Warts. These tumors are most common on the soles of the feet but like lesions are sometimes seen in the palms of the hands. Though insignificant in appearance they sometimes cause their possessors great annoyance.

Pathogenesis. What starts these warts is not known. They are seen as often in sheltered persons as in those much on their feet. They appear as corn-like, circumscribed, whitish lesions seldom elevated above the

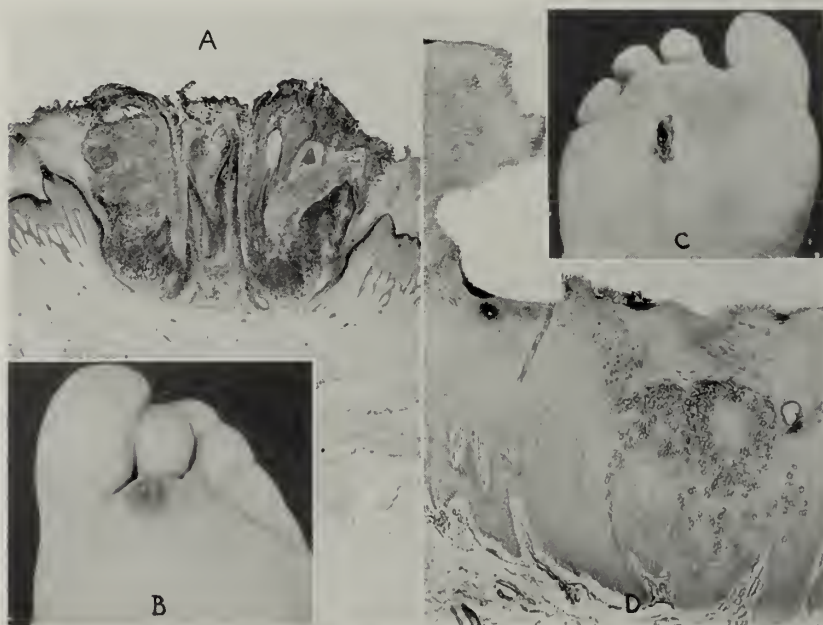


FIG. 38. Plantar warts. *A*. Circumscribed epithelial proliferation sharply defined against the adjacent epidermis, *B*. Circumscribed dense slightly elevated nodule; *C*. Depressed type. The site of the wart is a depression; *D*. The wart appears as an inverted corn surrounded by much thickened epidermis.

surface. The epithelium, instead of projecting above the surrounding surface of the skin, penetrates deeply into the tissue and by pressing on sensitive parts beneath causes great pain. They are clinically benign but are simulated by certain chromatophoric tumors which gives them an added clinical significance.

Pathology. The white hard sclerotic area is apparent on inspection and is approximately the same elevation as the surrounding skin. The surface is dense corn-like (*B*, Fig. 38). The density of the lesion, however, is not appreciated until an attempt is made to cut through it. Sometimes

the surface is marked only by a keratotic area. In some cases the site of the wart is marked by a depression (C, Fig. 38).

Histology. The entire tumor is made up of very dense keratotic epithelium (A, Fig. 38). They are sharply defined against the surrounding skin but the adjacent epidermis may show proliferations. The depressed type may present a wider area of epidermal thickening (D, Fig. 38).

Senile Warts. Naturally these tumors are most common in those of advanced years but not all senile warts are found in the aged. The term should be reserved for epithelial growths situated most frequently about

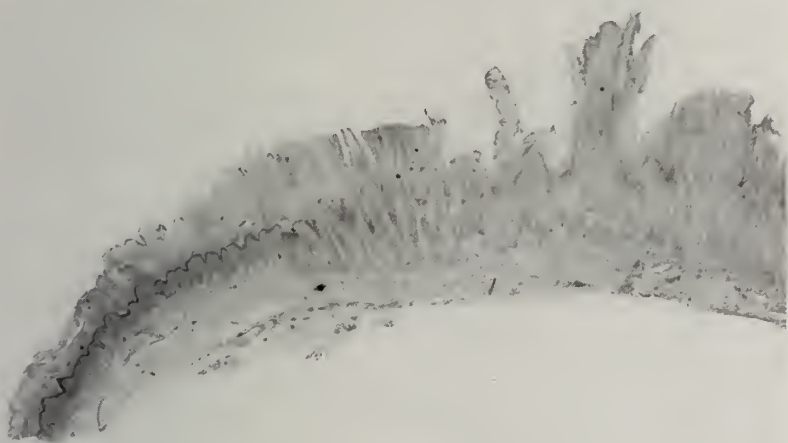


FIG. 39. Diffuse keratotic wart on temple, duration two years. M., age 56. The high hyperplastic epidermis diffuses gradually into the normal skin at the left. Removed, cured 18 years.

the face, neck, and hands of adults. Because of their not infrequent degeneration into malignant tumors they are of considerable clinical importance. This is particularly true of those occurring on the backs of the hands and on the face. They may be divided into the diffuse and circumscribed types.

Diffuse Senile Warts. The flat papillated warts, most common in middle life, which gradually suffuse into the surrounding skin, should be particularly regarded because of the type of malignancy they ultimately assume.

Pathogenesis. They begin as flat keratonized patches which gradually thicken. There is no dividing line between them and the surround-

ing normal skin. They are most common on the temple, the backs of the hands, and on the chest and back. They may be confused with the flat melanomas but are less circumscribed than melanomas (Fig. 39). They may remain quiescent for years but gradually increase in height and ultimately take on malignancy and become prickle-celled cancers, often

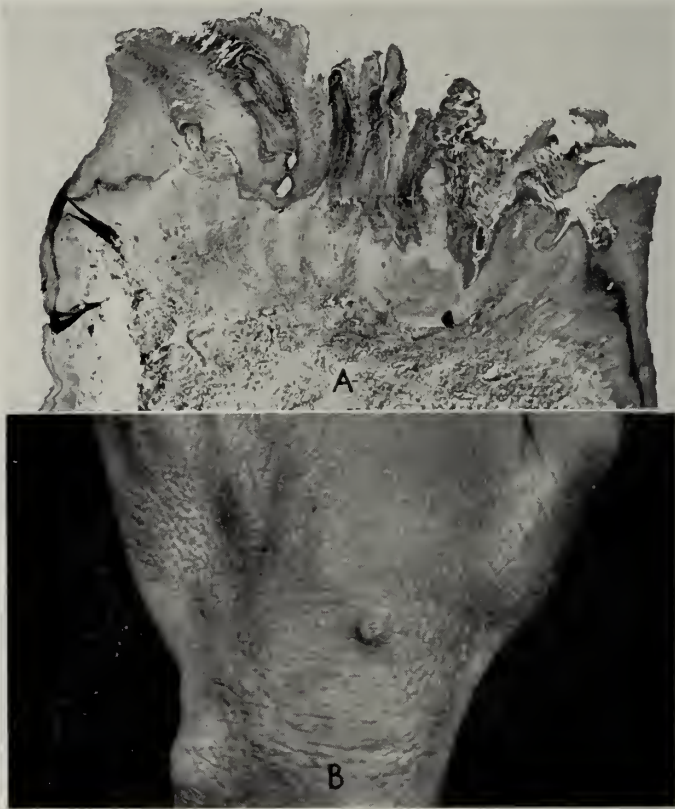


FIG. 40. Senile wart on back of hand. M., age 36. Two months' duration, sharply circumscribed. *A*, keratotic proliferation of the epithelium and some round cell infiltration at the base. *B*, clinical appearance of the tumor.

with early metastases. This is particularly likely to occur in those on the backs of the hands (Fig. 40). Sometimes these warts, notably those situated on the temple, may have the appearance of melanotic warts (*A*, Fig. 41) but the slide shows them to be entirely of epithelial formation (*B*, Fig. 41).

Pathology. Both palpation and section show them to be confined to the epidermis. Their epithelial nature is obvious from the gross section

(Fig. 40). Some are circumscribed and appear as though set into the skin like the plantar warts, or they may shade off gradually into the surrounding skin.



FIG. 41. Papilloma of the temple, present many years. It used to be flat but recently has been becoming higher. The tumor is horn-like to the touch, freely movable with the skin. Removed. No recurrence in one year. *B*. The tumor is made up of cornified epithelium undergoing proliferation but no invasion though backed by areas of round cell infiltration.

Histology. They are made up of dense epithelial papillations of varying height with unchanged dermal connective tissue (Fig. 39). If the dermal layer is infiltrated with round cells the precancerous stage has already begun (Fig. 40). The beginning malignancy is signalized by the invasion of the dermal layer by the proliferating epithelium.

Circumscribed Senile Warts. The circumscribed type of senile wart is more deserving of this designation for they are found commonly in the aged. They are distinctly lesions of the face but are found elsewhere.

Pathogenesis. The exciting factor of the papillary growth is not known. Likely there is some nutritional disturbance. Most of these tumors, to say the least, are glandular in origin, most commonly fat glands, less commonly coil glands. Though classed as senile they may have their origin in much earlier years. They appear first as shot-like lesions within



FIG. 42. Very early senile warts. *A.* M., age 60. Small shot-like tumor which developed within the past few months. *Insert*, a hyperplasia of the epidermis is flanked by a mass of fat glands. *B.* M., age 65. First noticed the tumor 4 years ago. It is elevated and the surface is reddened. *Insert*, it is covered with a normal epidermal layer, the tumor being made up of hyperplastic fat glands.

the skin (*A*, Fig. 42), more apparent to the touch than to the sight. They gradually become more elevated (*B*, Fig. 42) but twenty or more years may be required for them to become protuberant and globular and really to deserve the term of wart. They are not dependent alone on external irritation because they are found in sheltered regions. On the other hand papillomas, when situated where they are subject to irritation, as on the bridge of the nose where they are irritated by spectacles, are particularly prone to malignant change. Since fat glands form such a large part of their structure it is evident that many of them are dependent on developmental abnormalities of these glands. Their constant location about the face is additional evidence of a congenital anlage.

As the tumor develops the surface becomes reddened and may become ulcerated or the skin about the base may show increased vascularity. When they have reached this stage they are precancerous lesions.

Pathology. Rarely they are covered with hard heavy masses of epithelium which may be divided by fissures but most bosselated warts belong to the fibrous tumors. Usually the surface is covered by smooth epithelium (Fig. 42) but when they reach a more advanced stage the



FIG. 43. Adenomas of the face (senile warts). *A.* M., age 81. Growth present 8 months. Firm elevated, skin covering defective. *Insert* shows sweat gland adenoma. *B.* M., age 54. Small wart many years. Surface broke down several months ago. Border firm, adjacent skin normal. *Insert* shows squamous celled carcinoma on the basis of a fat gland senile wart.

epidermal covering is usually defective. When this is the case the benign stage has passed (Fig. 43).

Histology. The tumor mass, instead of being made up of proliferation of the papillary layer (*B*, Fig. 41), consists of subdermal masses, sometimes wholly of fat glands (*A*, Fig. 42), sometimes of sweat and coil glands (Fig. 44). Old senile warts which have remained unchanged may show areas of cell proliferation (Fig. 44). These commonly have the cell structure of basal celled epitheliomas. Whatever the source of these cells they are not derived from the basal cells of the skin. When they reach this last stage they should be classed as malignant even though they are yet

small and have shown no active proliferation. Tumors of like duration and external form (Fig. 43) may show astonishing variation in histological structure. In *Insert A*, Figure 43, the structure is that of a sweat gland adenoma while *Insert B*, Figure 43, is composed of hyperplastic squamous epithelium with a tendency to pearl formation. In the later type epithelium changes may be slight yet metastases may already have taken place. This type of wart is most commonly situated near the angle of the jaw or on the neck.

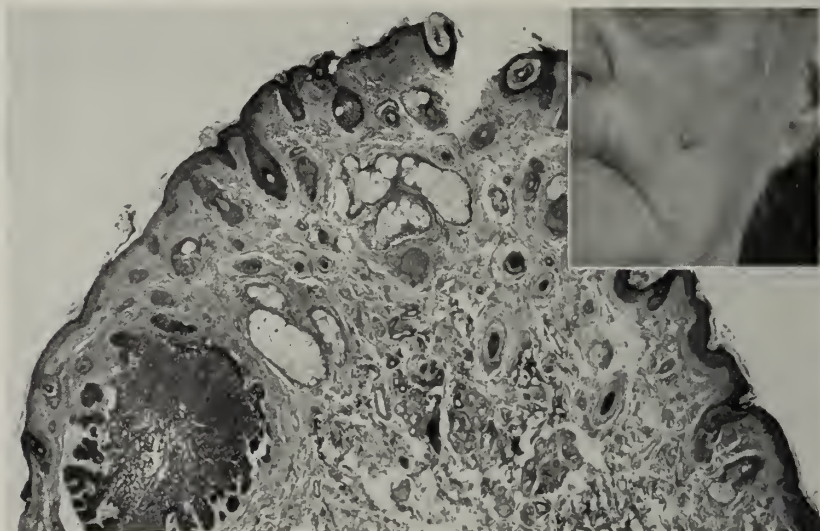


FIG. 44. Senile wart. Small wart of the cheek which has been stationary for many years' duration. Incidental finding; removed for purpose of study. It is made up of fat and coil glands interspersed by bundles of palely staining connective tissue. At the lower left there is cell proliferation of the basal cell type but at no point is it in contact with the epidermis. *Insert*, the wart one-half natural size.

Horny Warts. As a result of piling up of keratotic cells dense horny projections may be formed. They are usually seen in those beyond middle life and are located about the ears, lips, backs of the hands, and on the glans penis.

Pathogenesis. They begin as scaly patches which increase gradually in height without any change in the surrounding skin. They may remain unchanged for years but malignancy may develop about the base. This is most likely to occur in those situated on the hand, temple or neck.

Pathology. Their horn-like character is wholly characteristic. They may be flat and but moderately elevated (*A*, Fig. 45) or they may be

prong-like (*B*, Fig. 45). In some cases they produce veritable horns, difficult to cut with a knife.

Histology. The bulk of the tumor is made up of keratonized epithelium. The connective tissue about the base is usually unchanged except perhaps for a more abundant blood supply. If round cells are present the precancerous stage has arrived.



FIG. 45. Keratotic lesions of the skin. *A*. M., age 61. Has had a rough spot behind right eye for 30 years. Surface is keratinized. *B*. M., age 62. Horny wart on side of neck for 3 years, freely movable with skin. Similar lesion on back of left hand and on lower lip.

ADENOMAS OF THE SKIN

Both the sweat glands and the fat glands give rise to tumors. They usually appear as circumscribed senile warts though they may appear in earlier life.

Sweat Gland Adenomas. These are situated usually about the face, more rarely on the trunk. They are generally benign but may become malignant. One of my cases presenting a tumor of the upper lip recurred despite wide removal. It is quite possible that more than is



FIG. 46. Sweat gland adenoma of the face. M., age 71. Has noticed small wart on face many years. It has grown steadily for the last 2 or 3 years. It is now the size of a hazelnut, irregularly lobulated; the base is slightly constricted. It is soft elastic on palpation.

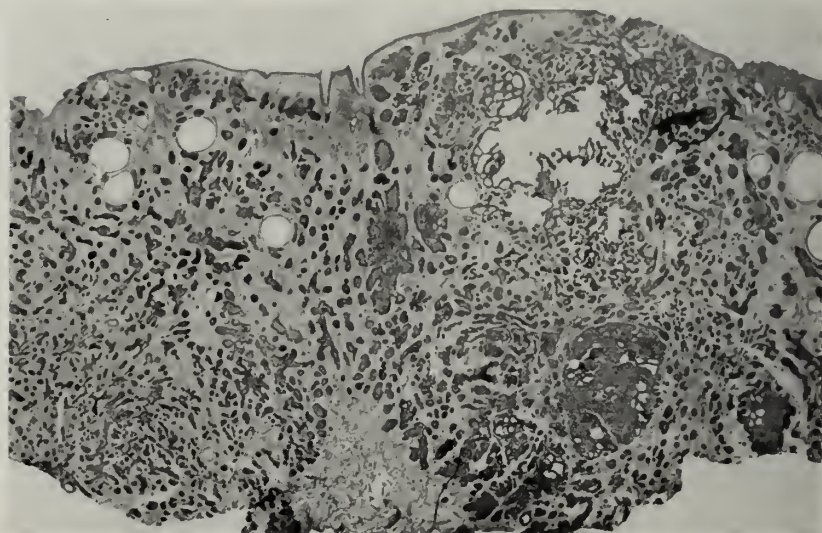


FIG. 47. Sweat gland adenoma undergoing malignant change. At top of figure dilated sweat glands appear. Below and to the right of the figure is a round area in which are many cystic spaces. Elsewhere branched columns of cells which resemble certain forms of basal celled epitheliomas.

generally believed of the slowly growing skin malignancies have such an origin.

Pathogenesis. These tumors begin as firm circumscribed tumors situated within the skin. In some cases they continue to lie deep but in others exhibit spheroid tumors projecting from the surface (Fig. 46). They usually are the size of a pea, less commonly the size of a hickory nut, but much larger ones have been reported. As they grow they may become cystic and when the contents is clear may resemble lymph-



FIG. 48. Fat gland adenoma of lower lip. M., age 36. Wart present several years. No complaints. Skin covering smooth.

angiomas. Such tumors may rupture, forming weeping ulcers and if malignant degeneration occurs a spreading ulcerous tumor is the result.

Pathology. Early they form firm nodules but they may be cystic as above noted. Their greyish color may be apparent through the skin. On palpation they seem to be well encapsulated but when cut across are seen to be diffused through the surrounding tissue. Sometimes comedo-like plugs can be pressed from them.

Histology. When the structure of the sweat gland is retained the recognition is easy. When cystic dilatation is pronounced or when the epithelium becomes heaped up they bear little resemblance to the original structure (Fig. 47).

Fat Gland Adenomas. It is generally stated that tumors of the fat glands are rare. This, I am sure, is a mistake. The reason for the failure to recognize them is that small warts are generally treated with contempt and when removed they seldom reach the surgical laboratory. Many of the spheroidal tumors of the skin, particularly about the face, develop

from these glands or from their aberrant anlagen. Pure fat gland adenomas are not uncommon. Careful search is necessary as malignant degeneration may be taking place in one part of such a tumor only. This statement will be amplified in the discussion of precancerous lesions. These tumors should not be confounded with the adenoma sebaceum of the dermatologists which are small multiple tumors of the sebaceous glands occurring in mental defectives.

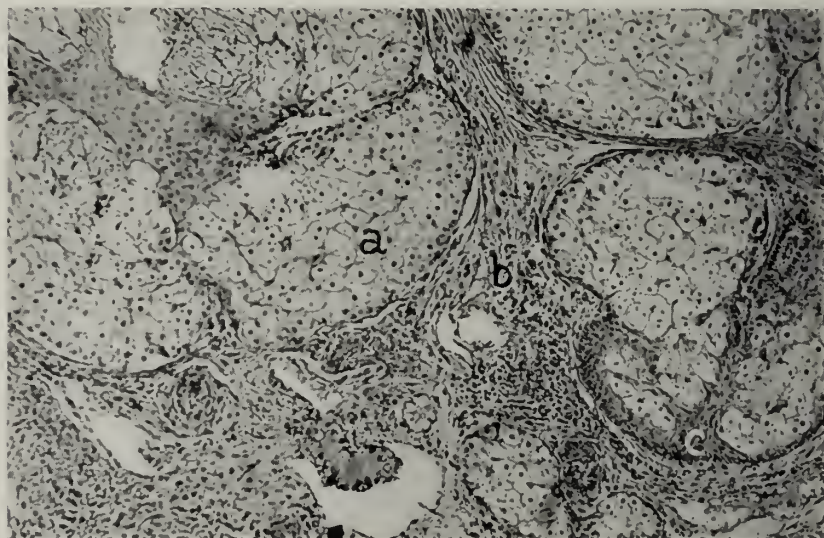


FIG. 49. Fat gland adenoma. The bulk of the tumor is made up of *a*, large cells with palely staining protoplasm and small deeply staining nuclei. These are surrounded, *b*, by bundles of fibrous tissue containing many round deeply staining nuclei. At *c*, are stratified squamous cells within the lobule of a fat gland which may have not developed into fat gland or fat glands which have undergone regressive changes.

Pathogenesis. Fat gland adenomas begin as slightly elevated globular tumors, obviously a part of the skin. The familiar rhinophyma must be recognized as a diffuse adenoma of the fat glands. They may attain a considerable size but may go on for years before malignancy begins. They cause no discomfort except that due to their situation and size.

Pathology. Fat gland adenomas present a firm elastic feel and are smooth or somewhat lobulated (Fig. 48). The color is generally that of the surrounding skin but may be brownish or reddish and may be traversed by numerous fine blood vessels. On section they are grayish in color and cut with the consistency of cheese though the surface is somewhat glistening.

Histology. The structure is that of the normal fat gland (Fig. 49). They are characterized by heavy connective tissue septa which is not fully appreciated unless special connective tissue stains are used. As they grow more rapidly the fat globules become less apparent until they are lost in definitely malignant states.

EPITHELIAL CYSTS OF THE SKIN

These ubiquitous little tumors are treated with contempt in most clinics and laboratories but nevertheless an astonishingly extensive literature has developed about them. Despite this, the exact nature of these cysts still is undetermined. Hence they furnish excellent material for independent research. For this reason these epidermoid cysts are accorded a detailed presentation usually denied them and beyond what their clinical importance would seem to warrant. They are the first objects which fall to the operative prowess of the pubescent surgeon. While their study usually ends, as most investigations do, in uncertainty, it is well worth while. The student can learn for himself the delights of forming his own opinion by the careful study of a considerable number of these little cysts.

While adopting the generally accepted division of epidermoid cysts into three groups I do so without enthusiasm and without understanding. First the wens: these are supposed to be due to the occlusion of outlet ducts of fat glands. There are such but they are not wens. I believe wens are sacculations of the epidermis intended to be fat glands but which never got to be such; the differentiation did not occur and the sacculations remained, little squamous epithelial-lined pouches, as we actually find them. Second, the epidermoids: these are sacs formed in lines of fetal development and are easily comprehensible as developmental anomalies; the explanation of their genesis is satisfactory. Third, the traumatic cysts: these are supposed to be due to the dislocation into the deeper structures of bits of epidermis due to some trauma. That such occur must be admitted from experimental evidence though one cannot help but suspect that some day someone will repeat these experiments and will encounter difficulties. It is all too simple. Be this as it may, such an explanation is unnecessary. Besides, the cases one sees do not provide any history of traumatism; not one in my experience. One often sees them in the palms of sheltered young girls who have never been the subject of any accident.

So let it be recorded here that of the hundreds of these cysts which have been observed in this clinic, or those which come to my laboratory in my pathology days, were all alike: simple epidermoid sacs.

Regular pathologists may find differences but the young surgeon may anticipate a happy life even if he fails to appreciate them.

Wens (Atheromatous Cysts, Epidermoid Cysts). These are cysts supposed to develop from occlusion of the outlet ducts of sebaceous glands. The most generally accepted theory is that through some means, as by the accumulation of dirt or by inflammation, the outlet duct of a fat gland becomes occluded and the retention of the secretion thus induced leads to the formation of a cyst.

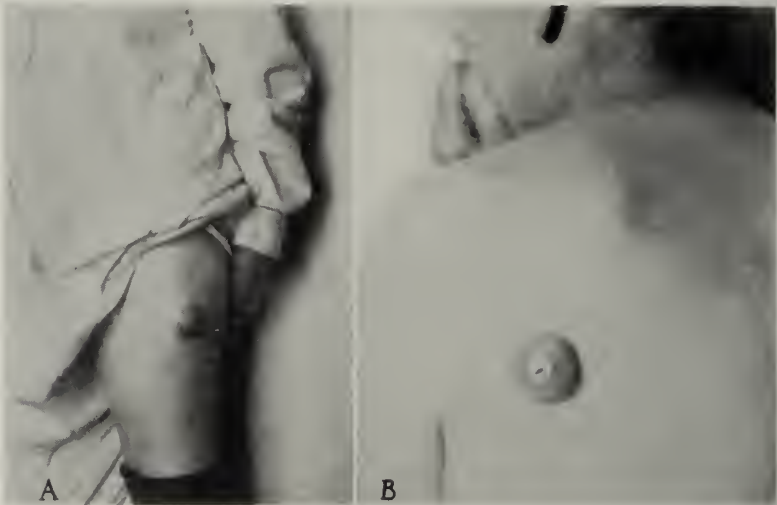


FIG. 50. Wens of the thigh and back. *A.* F., age 63. Cutaneous cyst of the thigh. Tumor present for 20 years, has grown more rapidly the last six months. The tumor is as large as a walnut and semifluctuating. The skin covering is reddish and thinned. *B.* F., age 60. Tumor on the back for nine years. The skin on the summit is continuous with that lining the cyst.

Pathogenesis. They vary in size from that of a pea to that of a walnut but very much larger ones have been recorded, however it must be remembered that the older authors included all epidermoids in one category.

Their common occurrence on the scalp is said to be due to the fact that this region is commonly the most dirty part of the body. This argument would hardly seem to apply to those individuals for whom a bath is but a recollection of the early weeks of post-natal life. In such cases there is no region of the body to which the superlative degree of dirtiness cannot be applied with justice. Wens often occur with unusual frequency in certain families. Of course the adherents of the dirty scalp theory of etiology may properly contend that dirty scalps are hereditary. But one must

needs suppress such an opinion in this clinic for wens are most commonly seen in matrons and frequently in those who groom themselves carefully. If this theory were correct one would expect wens of the face to be common but they are not.

They are attached to the skin but movable on the underlying tissue. In some cases one can demonstrate a duct leading to the surface of the skin. Microscopic study has demonstrated such instances, but this is also true in pilonidal cysts which are no doubt true epidermoids or dermoids, certainly not wens. This would be the case if they were due to cell dis-



FIG. 51. Wens of the scalp. *A.* F., age 56. Tumor of scalp for many years. A year ago it became inflamed, broke and discharged pus. It reformed and is now inflamed again. The skin covering is reddened, the tumor fluctuating. *B.* M., age 56. Small tumors of the scalp which have gradually enlarged to the present size. They have never caused trouble. They are soft, smooth and elastic.

placements during development. The most deeply lying cysts have no attachment to the skin. If the wens are due to occlusion of the outlet duct of fat glands one would expect that the cyst would be attached to the skin in all cases.

It is interesting to note that wens are sometimes covered by an attenuated skin quite like certain baldheaded sarcomas of the skin as described by Hertzler (*A*, Fig. 50). Furthermore the cell lining is so like the epidermoids lying over developmental folds that a very close association seems very probable. The wens of the cheek are usually located in line of one of the developmental clefts. It would seem therefore that there may be some relation between wens and certain solid tumors. In some cases there is a

continuation of the epidermis of the surface of the body with that lining the cyst (*B*, Fig. 50).

They are commonly discovered when small, pea size. They develop slowly, generally in the course of years, to be as large as hickory nuts, seldom as large as a walnut, but in rare instances much larger. In rare instances they develop malignancy. I have seen three of these, one on the cheek, two on the scalp.

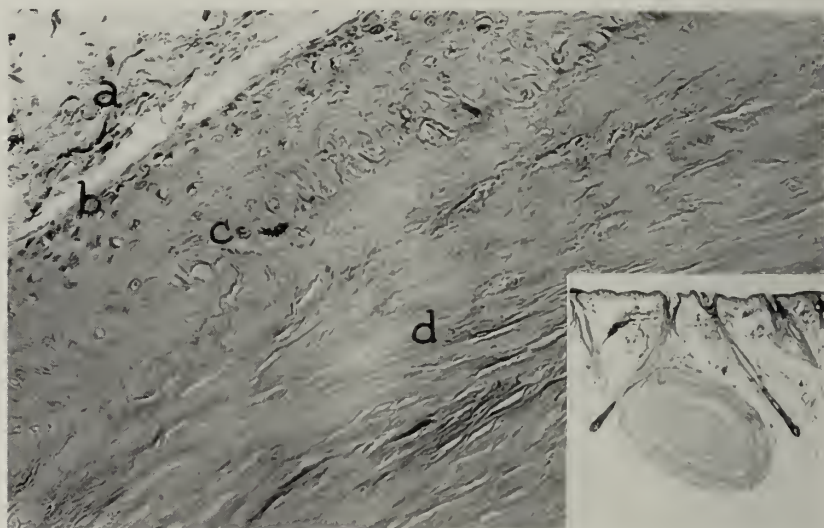


FIG. 52. Wall of a small wen: *a*, connective tissue of the cyst wall; *b*, large epithelial cells of the germinal layer some of which show bridges; *c*, epidermoid cell undergoing karyokinesis; *d*, desquamating epithelium which forms the contents of the wen. *Insert*, gross section of a small wen, magnified 4 diameters. It has no attachment with the overlying epidermis.

Pathology. Wens are usually globular, are rarely lobulated and confluent (Fig. 51). Often the covering skin is thinned (*A*, Fig. 51), but usually is smooth and glossy (*B*, Fig. 51). Frequently the hair over the surface is scanty. They are most common on the scalp or neck, less often on the cheek, back or chest and occasionally on the extremities. They may be solitary, but on the scalp are frequently multiple. They are firm when small, doughy when larger and fluctuant when they are breaking down. They cause no pain and annoy the patient only by their presence.

Wens are said to be attached to the skin because of the outlet duct of the fat gland, a retention cyst of which they are believed to represent. As a matter of fact the very small wens have no close relation to the epi-

dermis (*Insert*, Fig. 52). As they become larger they are closely associated with the connective tissue of the dermal layer. The lower part of the cyst wall extends into the subcutaneous tissue without any extensive attachment, the tissue being pushed aside as the cyst develops. The cyst wall obtains its nutrition from the region of its attachment to the skin.



FIG. 53. Dermoids of the temple. M., age 12. Tumor of the outer canthus of the eye. Soft, semifluctuating. Unattached to the skin. *Insert*, similar tumor in a child aged two years.

The cyst content is made up of cast-off epidermal cells. Rarely does it contain fatty acids and cholesterol crystals, and still more rarely calcareous deposits.

Malignant degeneration occasionally occurs, usually in the cells lining the cyst but it may take place in the covering skin. It manifests its presence as a hard ridge at some part of the circumference of the tumor. In some cases the entire cystic cavity is filled with epithelial growth which by destroying the surface produces a fungating mass. The tumors produced within the cysts are epidermoid tumors.

Calcareous plaques may form in the walls of the cysts. In rare instances the entire wall is involved in a calcareous infiltration and in small ones the entire cystic contents may be so transformed.

The cyst often becomes infected and ruptures through the overlying skin. Usually the opening closes and the cyst is soon reformed. Rarely the lining of the cyst is destroyed and a spontaneous cure results.



FIG. 54. Dermoids in mastoid and paranasal region. *A.* M., age 56. Small soft wart-like tumor behind right ear of many years' duration. Never caused any trouble. Surrenders it to please his doctor. *B.* M., age 56. Tumor beside nose many years. Had epithelial lining. Meningoceles sometimes point in this region.

Histology. The outer wall of the cyst is made up of connective tissue continuous with the lower dermal layer. The lining is a stratified squamous epithelium (Fig. 52). The superficial cells undergo a degree of hyalinization and lose their nuclei. The cells lying more deeply become progressively thicker as the outer layer is approached, the outer layer having well marked nuclei. These sometimes contain pigment (Fig. 52). In rare instances the epidermal layer of the skin may be demonstrated to be continuous with the epithelial layer lining the cyst (*B*, Fig. 50).

Epidermoid Cysts (Congenital Epidermoids, Dermoids). These cysts are called true epidermoids to distinguish them from the preceding. They occur in the lines of developmental folds and are generally accepted as

being due to some defect in development. They differ in a number of particulars from the more deeply lying dermoids. These will be considered in the discussion of the various regions in which they occur.

Pathogenesis. These tumors are most commonly found on the temple, at either canthus of the eye (Fig. 53), at the glabella, over the great fontanelle, beneath the chin, on the neck above the hyoid bone, over the sternum, etc. Small tumors over the mastoid process are common (*A*,

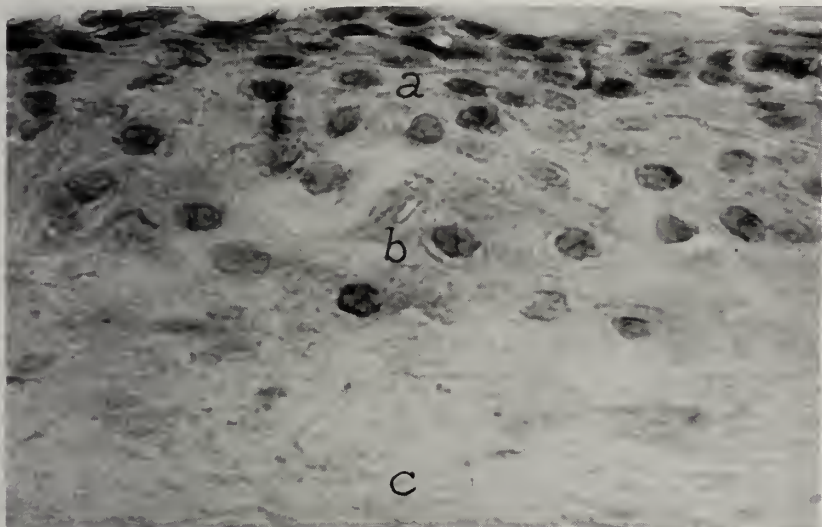


FIG. 55. Wall of an epidermoid cyst: *a*, stratum germinativum with well marked intercellular bridges; *b*, cells losing their distinctness; many show karyokinesis, terminating in *c*, the stratum corneum which furnishes the material which fills the cyst.

Fig. 54). Just beneath the inner canthus of the eye (*B*, Fig. 54) is a common site and it is noteworthy that meningoceles sometimes point here. In the middle of the cheek a cyst is not infrequently encountered and though it lies in the fissure line it usually is referred to as a wen. They generally attain a certain size and remain stationary. They are not attached to the skin, hence do not tend to become infected. When situated over the cranium the base may lie in a depression in the bone or in rare cases a part of the sac may lie within the cranium.

There is one type particularly worthy of emphasis, those occurring over the sacrum, the so-called pilonidal cysts. They seldom form tumorous enlargements, quite commonly have a communicating sinus to the surface. They cause trouble only when they become infected. They may be associated with globular tumors within the pelvic cavity. This aligns

them with the teratoid tumors. Sometimes these tumors are not exactly in the midline and are more closely attached to the skin, therefore correspond more closely to the wens, though anatomically they are the same. They are lined with squamous epithelium and quite commonly contain hair, therefore the term "dermoid" is applied to them. They contain all the layers of the skin including the appendages in contra-distinction to the epidermoids which contain only the epidermis and a fibrous tissue capsule.

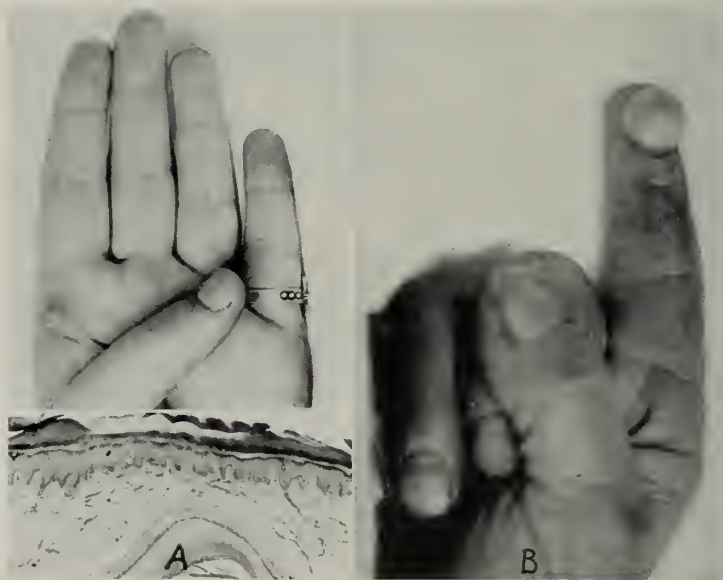


FIG. 56. Epidermoid cyst of the skin. A. F., age 16. Small tumor of palm of hand several years. No history of injury. B. M., age 46. Tumor on tip of right index finger, present many years. Recently it has become larger. Both these were lined by squamous epithelium. *Insert*, section through skin and cyst wall.

Pathology. Epidermoid tumors are always globular and protrude from the surface on which they lie. The overlying skin is smooth and usually unchanged and the attachment to the tumor is not intimate. This fact indicates only, in my judgment, that the embryonal displacement occurred at an earlier date than in the case of the wens.

The cyst wall is composed of a connective tissue capsule independent of the surrounding skin. The lining of the cyst is uniform and the contents a grumous material identical with that contained in wens. Very rarely they are the starting points of malignancies.

Histology. The lining membrane is composed of stratified squamous epithelium showing in many instances a papillary layer beneath, with

gradually thinning epithelium as the surface is reached (Fig. 55). The upper layers are usually in the process of exfoliation and show a distinct keratinization. The cyst content is exfoliated epithelium and structureless material. The basal layer of cells often contain pigment as is the case in the wens but much less commonly so. This would seem to indicate an earlier embryonal displacement.

Traumatic Epithelial Cysts (Implantation Dermoids). By this term is understood cysts which are alleged to be derived from epithelial masses

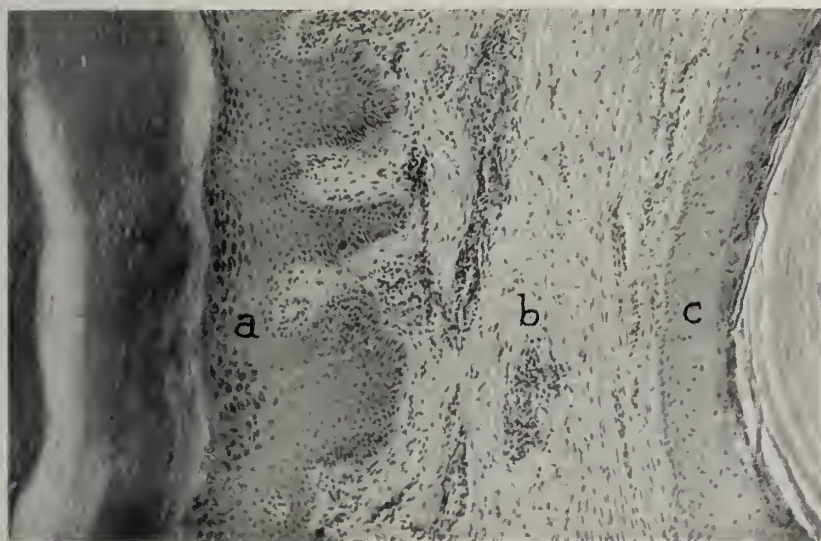


FIG. 57. Inclusion cyst of palm. Slide across the overlying skin and the cyst wall: *a*, epidermis of the palm of the hand; *b*, dermis; *c*, the cyst wall to the right of which is the stratified keratinized epidermal epithelium which entirely filled the cyst.

which have been displaced into the subdermal tissue by some antecedent trauma.

Pathogenesis. The presence of cysts containing material like the wens in regions where there are no fat glands, notably in the palm of the hand (Fig. 56), has made another explanation of their origin imperative. To explain their presence a number of authors, first of all Reverdin and Garré, assumed a traumatic displacement of epithelium into the depth of the tissue where they remained to form a cyst.

As to duration, the most of them come to clinical observation within 3 years after discovery by the patient but some have existed as long as 40 years. In none of my patients was the tumor ascribed to an injury and when questioned none could recall such an event. I once removed such a

cyst from a petite young lady who never had exposed her hands to so much of a trauma as contact with a dish rag. Nevertheless a number of writers maintain the correctness of the traumatic theory of their origin.

The experiments which have been performed to demonstrate the possibility of cyst formation are not convincing. While the possibility of a traumatic origin cannot be denied on histological grounds, such transplantations must needs be aseptic, a condition difficult to comprehend in the palm of the hand. If the hypothecated transplanted bit of epidermis should carry bacteria, suppuration and extrusion of the transplanted bit would inevitably result. That a traumatic transplantation of an aseptic bit of skin may happen is hard to believe. These tumors are confined almost entirely to the hand, though rarely they are found on the soles of the feet.

Pathology. These cysts lie just beneath the skin and are usually more or less intimately attached to it. They vary in size from a millet seed to a hickory nut or even larger. Not infrequently they have the peculiar dimpling of a thinned overlying epidermis commonly seen in wens (*A*, Fig. 56). Usually however the skin over the tumors is unchanged (*B*, Fig. 56). Rarely they are lobulated or multiple. I have seen them so large as to suggest palmar tuberculosis. When small they are distinctly firm but when larger they may have an elastic or doughy feel. They cause trouble chiefly by their mechanical presence. Seldom are they sensitive and but rarely do they suppurate.

Histology. Between the cyst wall and the skin is a layer of connective tissue quite independent of or continuous with the deeper layers of the skin. The connective tissue surrounding the cyst may contain cells so large as to suggest a neoplasm. The cyst wall itself is entirely epidermal in structure (Fig. 56). The histology may be described by repeating verbatim the histology of wens and epidermoids. This is particularly well shown in Figure 57. This shows perfectly the origin of the cyst contents from the scaling epidermis. Toward the lumen of the cyst the nuclei become more indistinct and cornification becomes complete and the cells lie upon each other like the peel of an onion. The central cavity may be entirely filled with keratinized epithelium. In some, particularly the smaller ones, there is no central cavity but the entire central mass is made up of epithelial cells making it appear like a huge pearl.

Literature

Epithelial Warts. Ziegler (*Lehrbuch d. allg. Path.* Vol. i, Aufl. 8, Jena, Fischer, 1895) divided the epithelial warts into (1) the congenital form which is related to congenital misplacement and bears a certain relation to the nevi, and (2) the senile form which is dependent on a local disturbance of epithelial growth.

Juvenile Warts. Payne (*British J. Dermat.*, 1891, 3, 186) had three warts develop upon his thumbnail after using it to separate a wart from the hand of a patient and Lantz (*Deutsche Med. Wchnschr.*, 1899, 25, 313) was able to reproduce warts by transplanting bits of wart under the skin of the back of the hand. Keen (*Jour. A. M. A.*, 1904, 43, 96) discusses the possible malignancy of warts.

Atheromatous Cysts, Wens. Though Boerhaave and Van Swieten (*Commentary upon Boerhaave's Aphorisms*, 1776, Edinburgh) anticipated the recognition of these cysts, Astley Cooper (*Surg. Essays by Cooper and Travers*, London, 1820, ii, p. 229, ed. 2) seems to have been the first to describe them adequately and to suggest the retention cyst theory and Virchow (*Virchow's Arch.*, 1864, 30, 221) accepted it. Paget (*Lectures on Surgical Pathology*, London, 1853) believed wens and dermoids to be one and the same thing. This is the most notable contribution to date. He noted that when the cysts are laid open the interior does not granulate but takes on the appearance of the surrounding skin. Foerster (*Handb. d. allg. Path. Anat.*, 2nd aufl., Leipzig, 1865, s. 362) regards wens as the lowest type of dermoid cysts. He says that they vary in size from a millet seed to the size of a double fist or larger. Rokitansky (*Handb. d. allg. Path. Anat.*, Wien, 1846, Bd. i, s. 314-317) was the first to suggest that wens are due to dilated fat glands. Borst (*Die Lehre v. d. Geschwülste*, Bd. ii, s. 840) also believes wens are retention cysts. Török (*Monatschr. f. Prakt. Derm.*, 1892, Bd. xiv, s. 169) believes there are definite embryonal displacements which account for their origin. In the very early atheromas, as Franke (*Arch. f. klin. Chir.*, 1886-7, 34, 859) pointed out, is shown evidence of cell proliferation. Chiari (*Zeitschr. f. Heilk.*, 1891, 21, 1897) believes they may form in sweat glands as well as sebaceous glands.

Congenital Epidermoids. Epithelial lined cysts in the line of the fetal folds seem to have been accepted as of embryonal origin without controversy. Remak (*Deutsch. Klinik*, 1855, 7, 1707) was the first to establish this theory. These cysts differ in some respects from the more deeply lying dermoids.

Implantation Dermoids. In order to explain their presence a number of authors, first of all Reverdin (*Revue med. de la Suisse romande*, 1887, T. vii, p. 121) and Garré (*Bruns Beitr. z. klin. Chir.*, 1871, xii, 641) assumed a traumatic displacement of epithelium into the depths of the tissue whence they remained to form a cyst. While Schweningen (*Charite-Annalen*, 1886, xi, 642), Kaufman (*Virchow's Arch.*, 1887, 107, 417) and Ribbert (*Deutsch. Zeit. f. Chir.*, 1898, 47, 575) believe they have demonstrated the traumatic origin experimentally. Frank (*Ibid.*) certainly is correct in stating that in most cases there is neither history nor evidence of trauma preceding the development of such cysts. True, Kisch (*Inaug. Diss.*, Leipzig, 1910) collected some 40 cases in which the cyst was alleged to have been preceded by a notable trauma. Christopher (*Minnesota Med.*, Sept. 1925, p. 607) reports a case in which a trauma preceded the development of the cyst 34 years. This cyst was situated over the terminal phalanx of the middle finger and caused a partial absorption of the bone. It is impossible in such cases to prove a causal connection. A number of writers have maintained the correctness of the traumatic theory of their origin. Notable among these are Johnson (*Trans. of Path. Soc. of London*, 1893, xlv, 146), Blumberg (*Deutsche Ztschr. f. Chir.*, 1894, 38, 613), Garré, (*Ibid.*) and Masse (*Comptes rendus de L'academie de sciences*, 1881, 799) and Hosch (*Virchow's Arch.*, 1885, xcix, 449). The majority occur in the palmar surfaces of the hand. Kisch (*idem.*) reports one on the buttocks and one on the temple. Pels-Leusden (*Deutsche Med. Wchnschr.*, 1905, 1578) advances the theory that a foreign body may cause a cyst by stimulating the cells of the sweat and sudoriferous glands to the formation of a cyst wall. There may be some truth in this. In the operation of rhinophyma where the growth is simply shaved off epithelization takes place rapidly, very likely by the participation of the cells of the fat glands.

CHAPTER III

Malignant Epithelial Skin Tumors

THOUGH malignant growths of the skin seem to be the best understood of all tumors, as a matter of fact, our knowledge regarding their pathology is still unsatisfactory from the surgeon's point of view. They range from the semi-malignant basal celled tumors of the face to the very malignant prickle celled tumors of the lip. The cause of this variation in malignancy has not been satisfactorily explained on anatomic grounds and the surgeon must lean heavily on topography, based purely on clinical experience, for his guidance. Why the relatively benign basal celled tumors of the skin of the face assume gross malignancy once they reach a mucous surface, as the conjunctiva or nasal cavity, cannot be explained from microscopic study, yet clinically we know it is so. Nor can the laboratory explain why prickle celled tumors of the skin are so much less malignant than like tumors of the mucous membranes. As is so often true in medicine the hot pursuit of a theory has obscured much of what had been learned by clinical experience. The surgeon must know much about tumors which the laboratory cannot explain. Therefore I have considered these tumors primarily from the clinical point of view, as the surgeon must always do. As a matter of fact it is much easier to classify these tumors to harmonize with clinical experience than with books on pathology and particularly those on dermatology.

Skin malignancies, in our pathologies, are generally divided into two groups: the basal celled carcinomas of Krompecher, and the prickle celled tumors of most authors—the acanthomas of Ewing, the deep cancers of Billroth. To these, as a clinical necessity, I am adding a third group, the adenoid. I take these to belong to the simple adenoid epitheliomas of the skin in Ewing's classification, a subvariety of the basal epithelioma. From the pathologist's viewpoint there can be no quarrel with this. Clinically they are so much more malignant than the basal celled variety that it is hoped by raising them to the dignity of a separate group the fact that they are more malignant may cause some to refrain from applying the simple therapeutic measures generally recognized as efficacious in the true basal celled type. To these belong the crateriform type of Ewing which are distinctly more malignant than the basal celled type and are in my judgment merely rapidly growing forms of the adenoid type. By such a classification one avoids the need of explaining why the basal cell

group sometimes have prickle cells, why they are sometimes destructive, and why they sometimes produce metastases.

While the basal celled tumors spring from the lower cells of the epidermis at many points simultaneously the group I have in mind develop in elevated wart-like lesions which at first have no contact with the epidermis at all. In my opinion they spring from the fat glands or the undeveloped anlagen of these, rarely from the coil glands. Those arising from the coil glands are less malignant and save for their rarity might deserve a separate classification. The same might be said of the cystic epitheliomas of Brooke. Both these are identified in the laboratory first, consequently they need not clutter the nomenclature of the surgeon.

The "precancerous lesion" is a much abused term. We mean by it lesions of which we are unable to say whether or not they are at present or will become malignant. They really belong with the malignancies because the line between the benign and malignant is so difficult to determine that in each group precancerous lesions should be considered as already malignant. To bring the precancerous lesions into the prominence which they deserve I am discussing them as introductory to the tumor groups to which they belong, for usually we are dealing with a lesion regarding which we are too timid to be sure of the diagnosis.

If the term "precancerous" is to be employed at all it should be used to designate lesions which we know full well are not malignant, but which may become so. They should be regarded as the small boy with a new gun who has not shot anybody—yet.

As one studies the small skin lesions, both the congenital and the senile warts, one becomes impressed with the fact that they are made up of cells so potential for mischief that they should all be classed as precancerous. Once they become agitated the term is no longer applicable because they are already malignant. It is only by accepting this as a working basis that we will come to manage these lesions in such a manner that a lessening of serious consequences will be achieved. Why tear our hair to inspire early diagnosis in cancers of the cervix when more deaths are caused by neglected or abused warts which at one time might have been certainly annihilated by a simple operation?

It would aid our clinical acuity if the basal celled tumors, the adenoid variety and prickle celled tumors of the skin should be excluded from the more malignant epithelial tumors of the mucous membranes. We may employ the term "epidermal carcinomas" for these, and reserve the unqualified term "carcinoma" for lesions of the lips and other mucous membranes, as well as those of breasts and other parenchymatous organs.

The reason for separating the basal celled lesions from both the glandular and epidermoid type is primarily practical. Basal celled carcinomas are curable by any mildly destructive measures, the curett and escharotic of the dermatologist, radium, etc., while the glandular and epidermoid types must have intelligent care lest they be stimulated to



FIG. 58. Precancerous basal celled epithelioma. M., age 51. Keratotic lesions on the right cheek for a year or more, covered with a white scab. Beginning basal cell proliferation.

greater malignancy. When a basal celled tumor destroys life someone has been inexcusably negligent and when a circumscribed glandular or a prickle celled carcinoma of the skin gets beyond control almost certainly someone has been playing with the devil. Each of these is easily recognized and easily cured in the beginning; there is no excuse for allowing them to get out of hand.

On the other hand, cancers of the lips, breast, and cervix and the like, destroy the majority of those they afflict despite the most vigilant observation on the part of the patient and the greatest skill on the part of the surgeon. We speak glibly of the importance of the early diagnosis of malignancies, which is very well, but after all it is the type of tumor which



FIG. 59. Keratotic lesions of the face. F., age 77. One over the bridge of the nose and in her right naso-labial fold were definitely basal celled carcinomas.

we encounter which determines the fate of the patient. The great need is the general recognition and adequate treatment of the less malignant types in the early stages. Wart specialists and not bold operators is the crying need in the practical management of malignant tumors of the skin.

The classification that will be followed here is: 1, the basal celled epitheliomas; 2, the adenoid epitheliomas; 3, the squamous epitheliomas—the acanthomas of Ewing.

BASAL CELLED EPITHELIOMAS

(Rodent Ulcer, Jacob's Ulcer, Krompecher's Carcinomas). These are the least malignant of the cancers of the skin. They are derived from the basal layers of cells of the epidermis and the skin appendages. They are most common on the face, particularly about the eyes and nose but may be found on the neck and trunk. They are characterized by insidious onset, slow growth, and slight disposition to form metastases.



FIG. 60. Slide from seborrhoeic patch on the skin, a so-called precancerous lesion. *a*, seborrhoeic scales; *b*, epithelium; *c*, blood beneath the scales; *d*, basal celled proliferation extending from the skin; *e*, tumor springing from a hair shaft; *f*, round cell infiltration.

The Precancerous Lesion. These lesions seldom occur in early life and are often multiple. They are most common in sandy-haired persons exposed to the elements and for this reason were formerly called sailor's cancer or sun cancers.

The typical incipient lesion is a scaly thickening of the skin. Small silvery white scales pile up, forming a slightly elevated lesion which resembles some of the seborrhoidal dermatoses (Fig. 58). The scales at first are easily removed, leaving a shiny pinkish base. As the lesions progress the removal of the scales leaves a slightly bleeding base much as follows the removal of the scales in psoriasis. In the multiple variety some of the lesions may be represented by tiny scaling areas, others may be definitely over the border between the benign and malignant (Fig. 59). These lesions may be single, multiple, grouped or discrete. Some forms begin beneath the epidermis and the surface becomes destroyed secondarily. The surfaces of these lesions are sometimes of a silvery color before the covering epidermis is destroyed. They present many other details which

differ from the typical basal celled epitheliomas. Some pathologists classify them as endotheliomas.

Microscopically these precancerous lesions show a thickening of the keratotic layer with a piling up of the basal cells (Fig. 60). It cannot be emphasized too strongly that the seborrhoeic surface is an expression of changes which have already taken place beneath and the lesion is already



FIG. 61. Basal celled carcinoma. M., age 60. Ulcerous lesion on cheek for several months. Superficial ulcer with granular base. Removed. Well after 7 years.

malignant. There is no general agreement as to just what the basal cells are. Suffice it to say that a study of these tumors shows that some are continuous with the prickle cells of the skin, others begin independent of them, apparently from inclusion cells independent of the epidermis, or growing out from hair shafts, as Mallory contends. The early scaling lesions begin in the basal cells, those beginning more deeply may elevate the epidermis before destroying it. There is no sharp dividing line between these and the glandular type. Wherever one places them it should be remembered that those beginning beneath are more potential for mischief than those which begin as keratotic lesions.

Having paid our respects to the so-called precancerous changes we approach the fully developed lesion. The dividing line obviously is expressive of the observer's knowledge and not the stage of the lesion.

The range of habitat of basal celled tumors is not yet fully established. Unquestionably they occur most frequently about the temple and face. They occur also on the chest and back. Here their presence requires additional study for they are more resistant to treatment and too commonly a more malignant tumor, that derived from epithelial papillomas, is mistaken for them. In other situations, for example in the cervix of the uterus, their existence should be denied on clinical grounds.



FIG. 62. Basal celled epithelioma of temple. M., age 49. Began as a small white elevated area about 4 years ago. It has gradually extended. In the past few weeks the skin over the center has been broken. Removed. Well after 6 years.

Pathogenesis. Beginning the description of the basal celled carcinomas at the point where the precancerous lesion merges over into malignancy one may say that it presents a small superficial scaly lesion from the surface of which pin-point hemorrhages occur when the incrustation is removed (Fig. 61). As the lesion extends the ulcer deepens and the increased exudate escapes on the surrounding skin. Many years may elapse before they become any considerable size. Less commonly now than formerly, one sees lesions which have grown 10, 20, and even 30 years and still remain superficial.

When they begin as flat patches the covering epithelium (Fig. 62) is destroyed sooner or later and a small ulcer remains. These are more apt to have a slightly elevated border than the variety just described. The cells are often closely associated with the glandular elements of the skin but are not derived from them. It is this type which has caused confusion with the glandular type next to be described. They are commonest on the temple and scalp and may after decades reach the size of the palm of the hand.

Sooner or later these tumors extend deeper and may reach the underlying bone and not infrequently destroy the entire thickness of the cheek, exposing the jaws and tongue. Such destruction may erode a vessel and cause extensive hemorrhages. Once the oral cavity is invaded secretions drain down the trachea and a pneumonia may result. Reduced nutrition of the patient incident to the difficulty of taking food and because of the painful, stinking mouth adds to the risk of this complication. There is no more repulsive sight in all human pathology than a face all but destroyed by one of these tumors.

But more common than the widespread superficial ulceration is the extension to the mucous surfaces. Once the tumor reaches a mucous membrane, as the conjunctiva or nasal mucosa, its character changes. It grows more rapidly and resists all treatment, quickly destroying the eyelids and exposing the malar and nasal bones.

The reason for this rapid change into malignancy obviously is to be found in the character of the underlying tissue. Dermal connective tissue is denser and more intensely acidophilic than that of the mucosa and therefore more resistant to the advancement of the wild-growing epithelium of the tumor. For this reason, too, these tumors grow more rapidly in the presence of inflammatory tissue as when secondary infection causes inflammation of the border of the ulcer. The reaction of the connective tissue lessens its acidophilic character thus reducing its ability to resist the advance of the tumor cells.

The readiness with which these tumors, particularly those beginning as keratotic lesions, respond to simple therapeutic measures is one of their most pronounced characteristics. Radiation with X-rays or radium, simple cauterization or even the internal exhibition of arsenic causes their disappearance. This has had an unfortunate sequel since tumors of greater malignancy have been treated similarly with disaster to the patient.

Pathology. Removal of the scaly covering reveals a superficial ulcer the base of which is covered with fine, firm granulations which bleed easily on manipulation. The border is slightly elevated, somewhat firm

to the touch but is never undermined, a condition so common in syphilis and tuberculosis.

Cross-section of the tumor emphasizes its superficial character. The unaffected deeper layer of the skin can be made out clearly. This explains the clinical fact that the early tumor is freely movable with the skin over the underlying structures, especially notable in the temporal region where skin plus tumor can be moved freely over the underlying temporal fascia. When small the skin with the tumor can be lifted up between thumb and

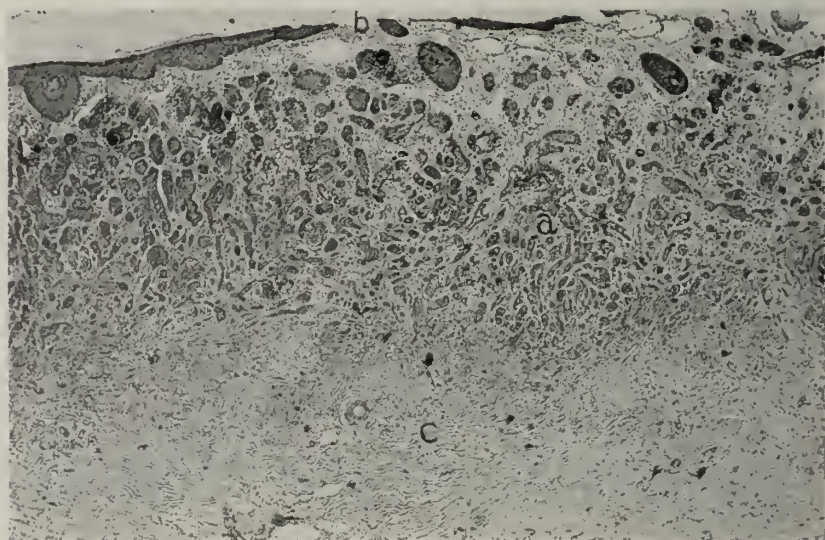


FIG. 63. Basal celled epithelioma. Many interlacing columns, some of which contain lumina, *a*. The skin is broken at *b*. There is an increased density of the subdermal tissue, *c*.

finger. The thickened border thus palpable suggests the indurated border of a chancre only that it is less marked and the adjacent skin is less affected than in the syphilitic lesion.

Histology. As previously stated the generally accepted opinion is that the tumor cells are derived from the basal cells of the epidermis (*d*, Fig. 60). Mallory is of the opinion that they are derived from the hair shafts (*e*, Fig. 60). This is certainly true in some cases and I believe the more one examines early lesions the more one becomes convinced that his opinions have been regarded too lightly. Some undoubtedly go out from hair follicles and actually seem to produce new hair shafts. Other tumors begin at numerous points and apparently independent of the epidermis. In these cases the covering skin has a silvery color (Fig. 63).



FIG. 64. Basal celled epithelioma. The cell masses show derivation from the basal cells at *a*. The cell columns form various cloverleaf-like masses, *b*. The subdermal connective tissue shows round celled infiltration. The tumor cells except at *a* are independent of the epidermal cells.

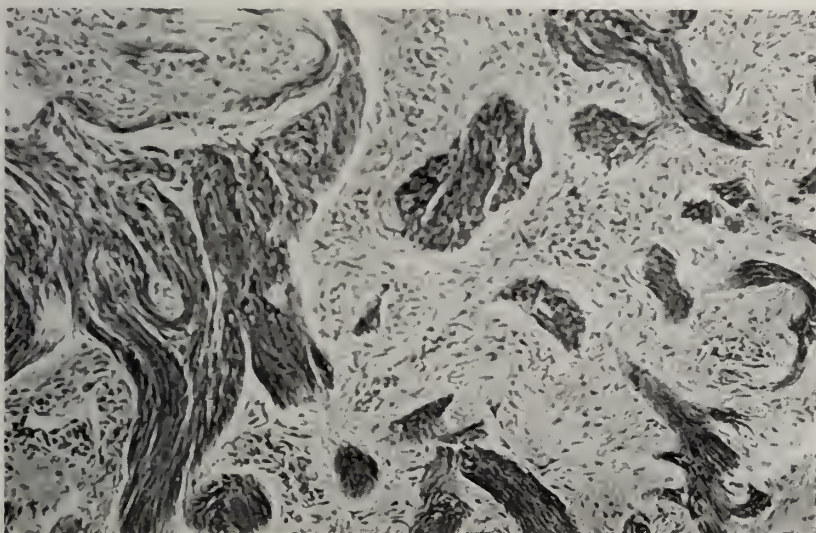


FIG. 65. Basal celled epithelioma showing spindleform cells. The clinical appearance of this tumor was typically basal celled and the most of the tumor was classical in structure. Areas such as these were found about the border of the tumor. The remainder of the tumor was made up of the usual form of cells.

In certain locations, such as the temple, in long neglected tumors there is an attempt at healing. Healing may occur in one point of the periphery as the ulcer extends in another but usually new epithelial-covered bands crisscross the ulcer, producing sometimes a very complicated network.

The typical cells of basal celled epithelioma are small and polyhedral, the nuclei small and deeply staining (Fig. 64). These tumors never form



FIG. 66. Rhinophyma. M., age 54. The nodulated areas were shaved off with a knife. Remained free from recurrence 16 years. Died of apoplexy.

pearls. When pearls are formed the diagnosis is wrong. The cells may be spindleform (Fig. 65) producing long prolongations; in fact, in studying some of these one feels disposed to wonder that some pathologist has not suggested a neurogenic origin.

The cell arrangement may follow several patterns. The most common is the formation of solid columns simulating an endothelioma. As a matter of fact many of them, particularly those of the scalp, often are diagnosed as endotheliomas. Less often a cystic or glandular formation may be simulated.

The connective tissue may undergo hyaloid or mucoid degeneration, producing a picture resembling cylindroma. Transitions between true basal celled epitheliomas and the prickle celled type have been described. In rare instances pearl formation and the formation of long spindle cells do exist side by side. In such cases one must pause to consider if they are really basal cell in origin. These tumors have the clinical disposition of prickle celled tumors.



FIG. 67. Glandular carcinoma of the cheek. M., age 61. First noticed small pimple 11 years ago. Slide shows carcinoma.

ADENOID EPITHELIOMAS

This group of tumors occurs chiefly on the face and neck, but is not uncommon in other regions. They begin as globular tumors which after a time undergo cell proliferation and destroy the covering skin and finally produce ulcerous lesions. I believe these are the lesions Hutchinson had in mind which he designated "crateriform ulcer," for certainly in the early malignant stages they are just that. They are more malignant than the basal celled carcinomas for they grow more rapidly when the ulcerous stage is reached and are more prone to form metastases. Therefore, for clinical reasons at least, these tumors should be accorded special consideration. Genetically many of them can be demonstrated as developing from fat gland adenomas, others from epidermoid cysts, less commonly from the sweat glands. Many of them seem to spring from undeveloped embryonal cells, possibly fat gland anlagen which failed to form glands.

In many of the little tumors a part is fat gland, a part masses of epithelial cells. It is impossible to say whether this represents the final stage of attempted development or whether the cell masses have resulted from changes in a previously completely developed fat gland.

Precancerous Stage. These tumors are most common about the temples of patients at or beyond middle life and consequently have been designated senile warts. They may exist many years without change.



FIG. 68. Adenoid carcinoma. M., age 60. Had a wart in front of ear for a number of years. It was destroyed by acid four months ago. Metastatic glands in the neck.

They seldom become as large as a hazelnut. Spontaneously or as the result of accidental or therapeutic injury the surface ulcerates. Only rarely do they manifest positive evidence of malignancy, such as metastasis, before ulceration begins. They find their counterpart, both clinically and pathologically, in fat gland adenomas of the nose. These when diffuse represent the well known rhinophymas (Fig. 66).

Pathogenesis. As the growth progresses from simple adenoma into a positive malignancy the epidermis about the base of the wart becomes

reddened and the surface becomes hyperemic and thinned (Fig. 67). On ulceration an irritating fluid exudes, producing a scab. When irritated they may produce metastases relatively early (Fig. 68). More commonly they tend to wide ulcerating lesions, often undermining the skin and forming hideous ulcers before metastases form (Fig. 69). The widely destructive



FIG. 69. Adenoid carcinoma of left temple. M., age 60. Small lesion on cheek for 20 years. Began to enlarge rapidly five months ago. The skin over the tumor is in part ulcerated, in part intact. The tumor was attached to, and was removed with, the temporal fascia.

lesions, now less commonly seen than in former years, were derived from circumscribed warty tumors and not from the seborrhoeic lesion (Fig. 70). These tumors form nodulated bleeding masses of slow but persistent growth. The fascia and muscle are invaded and even the bone is destroyed.

Analogous lesions about the nose produce protruding globular or diffuse tumors. They also are prone to ulcerate (*A*, Fig. 71) but metastases may form before ulceration takes place (*B*, Fig. 71).

Tumors of like clinical import may develop from epidermoid cysts, the so-called wens, showing the close relationship between the cysts

developing from the anlagen of the fat glands and the fat glands themselves.

As the ulcer progresses the lesion becomes adherent to the underlying fascia. The border is thick, hard, often nodulated, and fine dots representing pearls can often be made out with the naked eye. The ulceration produced by these adenoid epitheliomas resemble somewhat the ulcers



FIG. 70. Ulcerating adenoid carcinoma of the face. F., age 53. For a number of years she had a wart in front of the ear. It began ulcerating 5 years ago and has gradually attained its present size. The fungating mass pushes aside the relatively uninvolved skin.

produced by basal celled tumors but on the whole is more massive and extends more deeply than the basal celled type. The ulceration progresses more rapidly and what is more important, tends to invade the neighboring lymph glands.

They are less malignant than the diffuse prickly celled type, the acanthomas, about to be described. One reason for this may be the connective tissue normally surrounding the fat gland lobules. At any rate the growing tumor destroys the covering skin before it invades the sub-

cutaneous tissue—the opposite is true of the diffuse variety. These tumors occur not uncommonly about the angle of the mouth. They are more malignant here than elsewhere, due no doubt to the rich blood supply in this region. They invade the cheek deeply and sometimes form tumors protruding beneath the mucous membrane of the mouth. Even when widely excised, including the whole thickness of the cheek, they tend to recur (Fig. 72). These approach the lip cancers in malignancy,



FIG. 71. Adenoid epithelioma. *A.* M., age 73. Ulcerating glandular carcinoma of the nose. Began a year ago. Had metastasis in the neck. *B.* M., age 76. Had small warts on nose for 20 years. Began to grow rapidly during past year. The growth on tip of nose showed only fat glands. The nodule on the left was malignant; removed; recurred with metastasis.

and save that they so closely resemble the milder type in the beginning, they had best be included in the mucous membrane carcinomas of the lip.

Pathology. The early lesion is firm, circumscribed and protrudes above the surrounding normal skin. Even when the stage of malignancy is reached, even to the formation of metastases, the skin may not be affected. Their sharply defined border distinguishes them from the basal celled type and the acanthomas (Fig. 73). After they ulcerate the border is elevated and the surrounding skin is hyperemic, due to secondary infection rather than to the growth of the tumor. Sometimes the border is distinctly nodulated (Fig. 70). The base of the ulcer is grossly granular, bleeding freely when injured, and, particularly in the later stages, cov-

ered with a dirty stinking exudate. As they extend more deeply the fascia is invaded and the tumor is immovable. Even the bone itself is not respected and superficially eroded bone may form a part of the base of the crater.

On cross-section the circumscribed nature of the tumor in the beginning is emphasized. The skin covers the lesion and suffers by invasion



FIG. 72. Malignant adenoma of cheek. M., age 60. Following wart on cheek a tumor with open top developed. Resected. Recurred one year later. Wide resection of whole cheek with flap graft. Recurrence in neck. Insert, slide from first operation—squamous celled epithelioma.

without active participation in the destructive process. The result is the diameter of the tumor exceeds to a considerable degree that of the skin defect. This is the distinctive gross characteristic of these tumors and should warn the surgeon (and the dermatologist) that he is not dealing with a simple basal celled tumor. In more extensive lesions the underlying fascia becomes a part of the ulcer. It is this type which is particularly prone to develop or retain bridges of skin across the surface of the ulcer, indicating again the relative independence of the skin from the

malignant process beneath. Even after they have destroyed wide areas of skin they still are not a part of it. The border still is sharply defined where the tumor begins. When cut across, the skin is seen to be a part of the tumor. The cross-section shows the tumor to be well circumscribed in the beginning.



FIG. 73. Glandular carcinoma of the neck. M., age 56. Tumor on the side of the neck 5 or 6 years ago. Applied carbolic acid and sulphur a few months ago and the skin ulcerated. The tumor is freely movable with the skin over the underlying fascia.

Histology. In many tumors the cells may be seen to go out directly from the fat cells (Fig. 74). One can often see the transformation into the malignant state in the familiar rhinophyma. One part of these tumorous masses may retain the typical fat gland structure while another is distinctly malignant (Fig. 75), proved so by recurrence and metastasis in the neighboring lymph nodes. The characteristic thing is the development of the tumor masses under the surrounding skin without directly invading it for a considerable time (Fig. 69). Sooner or later the skin is



FIG. 74. Glandular carcinoma developing from fat glands. *a*, The fat gland structure is maintained; *b*, partial change in the fat gland and fat gland anlage. The small cells about the fat gland cells have the same morphology as basal cells but have greater growth potentiality.

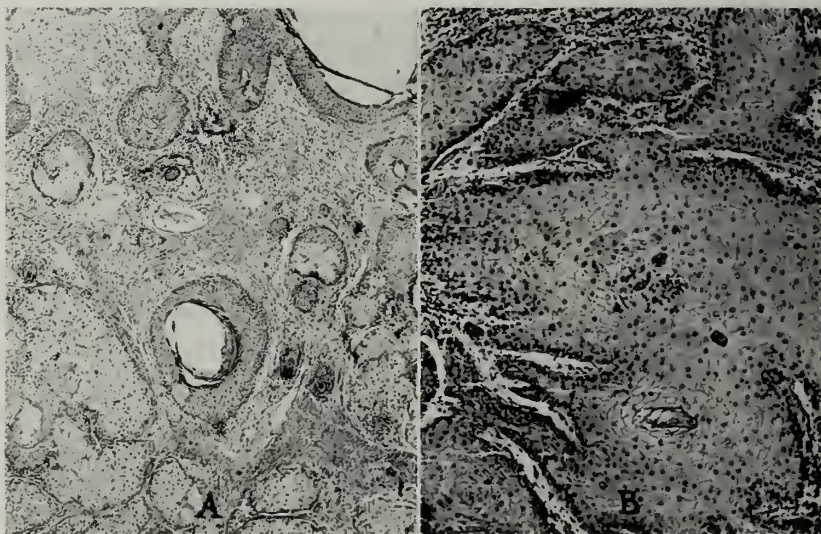


FIG. 75. Slide of adenoma of the nose. *A* shows fat gland structure. Typical fat glands are shown in the lower part of the picture while above there is some epithelial proliferation. *B*, gradual formation of squamous celled carcinoma with tendency to pearl formation.

destroyed and first a crateriform tumor is formed, then an ulcer; this proving microscopically facts already obvious from clinical examination.

In many cases the cell columns lie closely together in masses and do not form a network. Sometimes in the slowly growing there is a tendency to cyst formation. The cells, particularly in the early stage, are large, palely staining and may contain fat drops. Pearl formation is not common though sometimes noted (*Insert*, Fig. 72). The cells are sometimes smaller and more deeply staining, simulating those of the basal celled

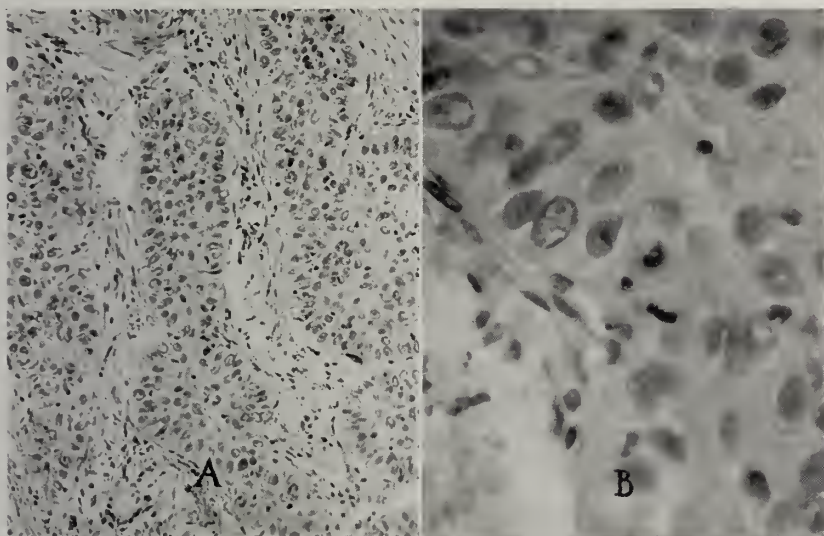


FIG. 76. Slide of fat gland carcinoma which had been irritated by caustic. *A*. Large cells formed into columns with considerable pale protoplasm. *B*. Same, high power. The ovoid nuclei with deeply staining nucleoli. One mitotic figure appears in the center of the cut.

type, but they do not form spindle cells as is often observed in that group. It is their development independent of any basal cell area that is distinctive in the last analysis, rather than any dependable histological differences. Sometimes outside the circumscribed tumors there is a limited basal cell proliferation. The metastases lose all suggestion of any relationship to basal celled tumors. Mitoses being frequent, the cells are large and intensely staining (Fig. 76).

PRICKLE CELLED CARCINOMAS

(Acanthoma—Ewing). This group differs from the preceding anatomically in that they develop from the prickle cells of the skin, consequently they are from the beginning part and parcel of the skin. Except

for its unfamiliarity to surgeons the term "acanthoma" would be preferred to designate this group of tumors. It would automatically separate them from the more malignant tumors of the mucous membranes and parenchymatous organs.

Clinically these tumors grow more rapidly than the types just considered, and tend more to form metastases. Microscopically they are characterized by pearl formation. They vary in their malignancy depending on their point of origin. Those developing in old scars and pre-existing skin lesions are relatively benign. Cancers produced by frequent exposures to the X-rays, as seen on the hands of all too many of the pioneer

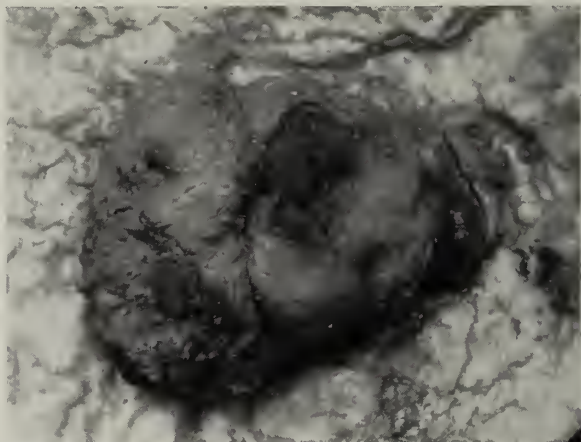


FIG. 77. Fungating carcinoma in a scar from a burn 44 years before. Excised. Has remained cured now 20 years.

X-ray operators, represent in fact an experimental form of acanthoma. In them one can trace the gradual change of the epithelium from the normal into the malignant. Fortunately malignancies due to this cause have now become a thing of the past. However, the lesson they have taught should not be forgotten for they permit the study of the early histological changes of malignancy, not possible in any other lesion.

Because the mucous membrane carcinomas are of such great malignancy and vary so much in detail according to their location, they will be dealt with in detail in the consideration of the pathology of the region in which they occur. This is imperative for in them the all-important question of metastases is always uppermost and this is largely a problem of topographic anatomy compelling a regional study.

Precancerous Lesions. The precancerous lesions have a very wide range of possibility. Old epithelial papillomas, or their counterpart, the

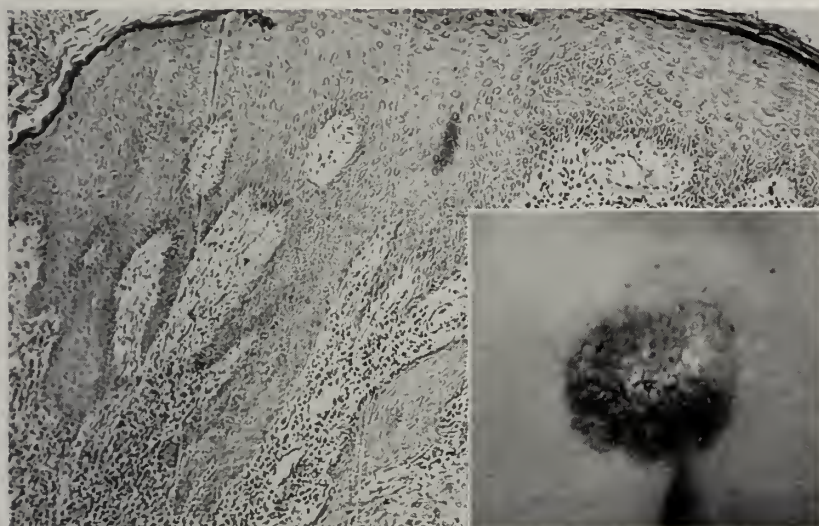


FIG. 78. Bowen's disease. The epidermis is thickened by hyperplasia of the germinal layer. Marked round cell infiltration about the proliferating epithelium. *Insert*, M., age 77. Red weeping lesion over sacrum 7 years. Elevated, papular; some incrustation in center. Removed by excision, skin grafted in defect. No recurrence.

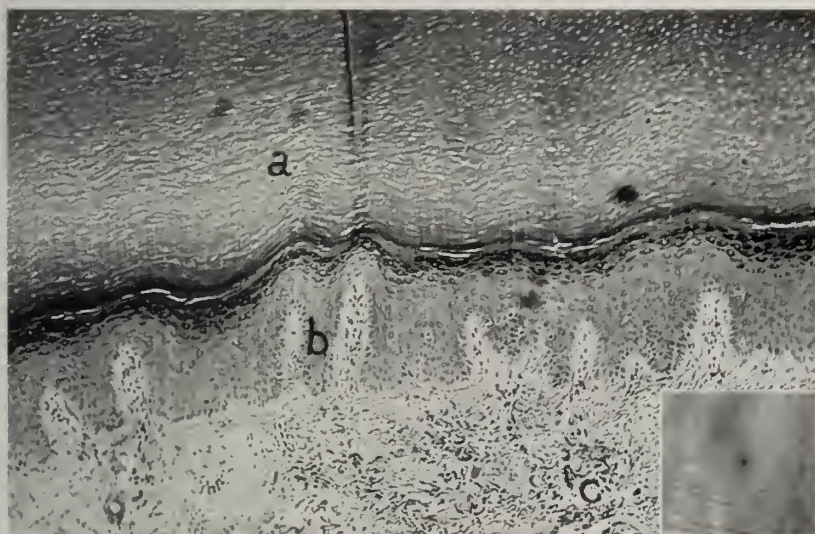


FIG. 79. Slide of early keratosis of dorsum of hand. The horny layer, *a*, is much increased; *b*, the basal layer moderate proliferation; round celled infiltration, *c*. *Insert*, gross lesion, actual size. It is more evident on palpation than by inspection. Lesion noticed while shaking hands. Patient had not noticed it.

cutaneous horns, commonly form the starting point for these tumors. Their change of character is signaled by a reddening and induration of the skin surrounding their bases. Ulceration indicates a malignancy already in progress.

Old ulcers and scars often are the starting point of epithelial proliferations. These are so hemmed in by dense scar tissue that though they may, because of their histological structure, be called malignant by courtesy, clinically they hardly deserve such a distinctive designation. They

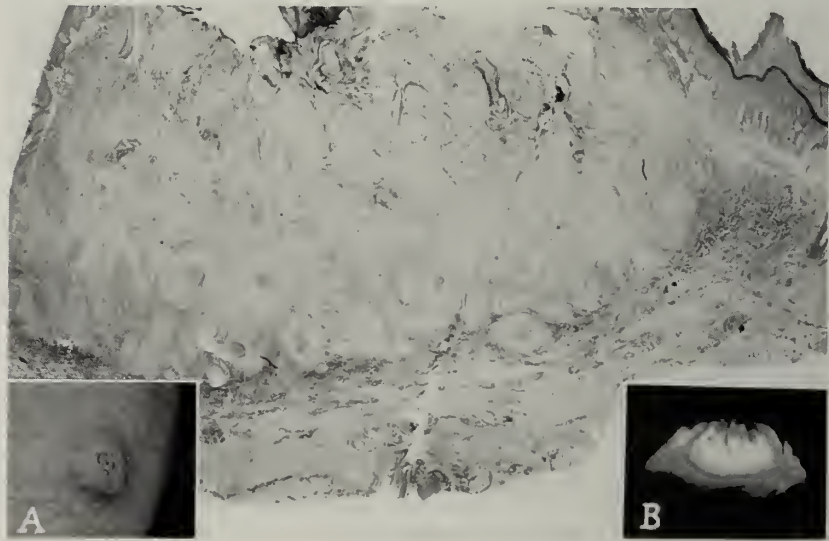


FIG. 80. Slide of papilloma on back of the hand. Well circumscribed but there is some cellular infiltration in the dermal connective tissue. The tumor is hard, epithelial in origin and shows a tendency to pearl formation. *Insert A* shows the gross, and *B*, the cross-section. The tumor is made up of cell nests which are fairly well defined from the surrounding tissues.

are the ward heelers among malignant tumors though the early beginnings resemble the more simple forms of epithelial hypertrophies. It is only those forms which form elevated protrusions above the surface of the old scar that require serious consideration. They are very rare (Fig. 77).

Perhaps Bowen's disease might be included here. This disease is characterized by the formation of firm, pinkish or reddish patches, occurring most commonly on the back. The surface is covered with thickened epithelium which produces round nodulated elevations (*Insert*, Fig. 78). The surface of these nodules may become abraded and the oozing resulting produces dirty grayish scabs. Histologically they form down-

growths of the epidermis which show but little change in cell type but the round cell infiltration is pronounced (Fig. 78). When removed and the denuded area is covered with skin grafts the patient is cured.

The back of the hand furnishes material for the study of the early precancerous lesions. Tiny keratoses scarcely visible (*Insert*, Fig. 79)



FIG. 81. Carcinomas of the back of the hand. *A.* M., age 56. Mass protruding above surrounding skin, surface fissured. Not attached to deeper structures. Has been developing a year. *B.* M., age 63. Ulcerous mass of 15 months' duration. Fixed to the deeper structures. Axillary metastases present.

are attended not only with thickening of the upper layers but also by activity in the basal layers. This, together with the round celled infiltration in the corium, furnishes a picture of the earliest lesion of this type of tumor (Fig. 79). These tumors may become of some size before unrestricted growth begins (Fig. 80).

Pathogenesis. Carcinomas developing from pre-existing lesions first show their disposition to grow by a hyperemia and thickening about their

bases. The most common sites for these lesions are the temple and back of the hands. In the former site there is usually a flat horny wart which may remain unchanged for many years. Those on the hand begin as small keratotic areas which may form elevated nodules before ulceration



FIG. 82. Prickle celled carcinoma of the temple. M., age 65. For many years he had a flat wart on the temple. During the past year it has ulcerated producing a large flat ulcer. *Insert*, the epithelial columns can be made out in the gross.

and wide invasion takes place. When the primary lesions break down, ulcers (Fig. 81) or elevated more or less nodular tumors are formed (Fig. 82). These may progress and involve wide areas, resembling in this the basal celled tumors, before metastases form but quite as often these are more likely to show real metastases surprisingly early. This is particularly true of those which develop on the backs of the hands.

Diffuse carcinomas which develop on old ulcer bases or other skin lesions are of exceedingly slow development, hardly advancing perceptibly from month to month or even from year to year. The border of the ulcer suggests a malignant structure; it becomes harder and the tissues beneath more deeply infiltrated. There is a peculiar hardness which in itself is all but pathognomonic. An ulcer usually remains but a protruding mass may form which may again break down, producing a combination of protruding mass with ulceration (Fig. 77). The skin surrounding



FIG. 83. Cell changes in early epithelioma of the skin: *a*, small, more deeply staining cells which have lost their prickles; *b*, cell nests; *c*, round cell infiltration in advance of the proliferating epithelium.

the lesion may be hyperemic, resembling an inflammatory lesion. When secondary infection occurs, as it most inevitably does, there is irritation of the surrounding tissues, the combined result of the growing tumor and bacterial invasion.

The typical skin cancers rarely develop on the base of old ulcers. They are more apt to form in the scars of traumatic or varicose, tubercular or syphilitic scars. According to the literature, in such cases they sometimes show considerable malignancy, destroying the more deeply lying tissue, and rarely even form metastases.

X-ray malignancies form an interesting type of skin cancer. They are of two types, varying much in clinical significance. Those following a single X-ray burn, as after massive treatment of deep therapy, and those resulting from continued irritation, as in the hands of X-ray

operators. The former parallel the scar cancers and are benign while the latter are relentless and ultimately destroy the victim.

Pathology. Hardness and infiltration together with a tendency to bleed on slight trauma are the essential features that indicate malignancy in epithelial tumors. To the experienced touch the peculiar hardness is distinctive. Cancer nests may be apparent to the naked eye at the border of the ulcer. They appear as grayish white dots in the redder background.

Epithelial malignancies are not circumscribed. They shade off into the surrounding tissue. They tend to become fixed to adjacent structures.

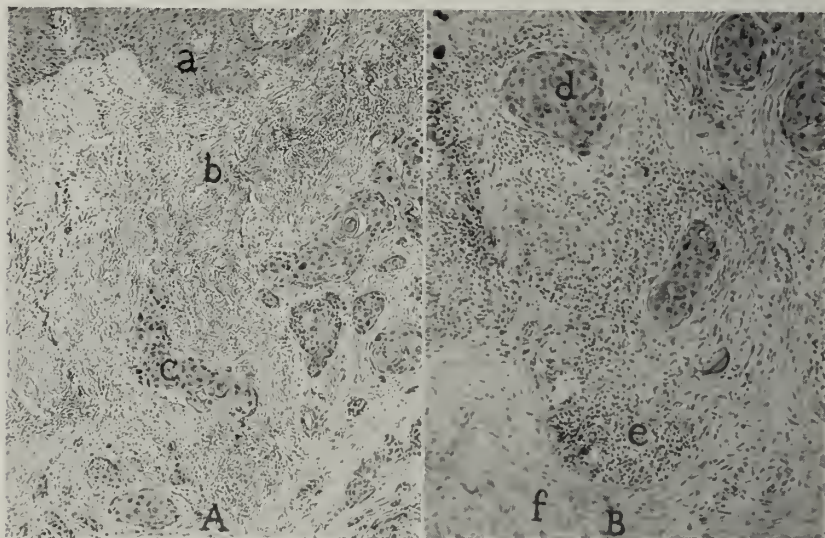


FIG. 84. Slide from X-ray malignancy of very slow development. *A*. Superficial part: *a*, proliferation of the epithelium, *b*, flanked by palely staining fibrous tissue infiltrated by round cells; *c*, cancer cells with the tendency to pearl formation. *B*. Continuation of *A*: *d*, cell nests which still retain their prickles; *e*, round cell infiltration; *f*, degenerated tissue which has lost its acidophilic stain-ability.

The neighboring lymph glands become involved sooner or later in all skin cancers. The cancerous lymph gland is characterized by its distinctly hard shot-like feel. The metastases into bone, parenchymatous organs, brain, etc., are seldom encountered in skin cancers. The destructive character of the initial lesion together with the lymph gland metastases usually terminate the life of the patient.

Histology. In skin cancer the elemental factors of early malignancy may be observed in its simplest form. Three changes occur which we teach sophomores (Fig. 83): 1. As the cells develop they revert to the embryonal stage. They lose their prickles, are smaller and their nuclei

stain more deeply with basic dyes. 2. Separate nests of cells, disassociated from the primary tumor, form in the connective tissue spaces. These are the cancer nests. The theory of disconnected cancer growth does not apply to this type of tumor. These cell nests quite commonly undergo extensive keratinization forming the so-called pearls. When they are found they are all but distinctive but they are not found in all cases. They may even be found in the secondary tumors in the lymph glands. 3. Round cell infiltration. Groups of round cells form about the advancing cell nests. This is apparently nature's attempt at limiting the growth of the tumor by the production of a barrier of connective tissue. They are to the growing tumor cells what the federal agents are to the booze runners. The resistance offered is purely theoretical.

It is necessary to distinguish between the round celled infiltration due to the malignant tumor growth and that due to secondary infection. In the latter the infiltration is most intense near the surface of the tumor and round cells are intermingled with polynuclear cells. The round celled infiltration from the tumor growth on the other hand is located between the advancing border of the tumor and the underlying connective tissue and is made up wholly of round cells. One of the characteristics of carcinomas, as already mentioned, is the stimulation to the formation of connective tissue. The nature of this is usually obvious but in rare instances it is so marked as to cause some doubt as to the nature of the tumor. Perhaps this stimulation may reach the degree of real sarcoma structure but the straddling diagnosis of sarco-carcinoma should be avoided. We must admit that such tumors do occur but hardly in the surgical laboratory.

As the cells lose their prickles and become more deeply staining the rate of growth increases. Cell nests with pearls surrounded by connective tissue represent the effort to produce normal epithelium. The center is formed by keratonized cells, surrounded by more or less well developed prickle cells beyond which are the basal layers. At the advance border the round celled infiltration is evidence of the conflict between the tumor cells and the defensive forces of the connective tissue. At the advancing border of the tumor the connective tissue has lost its typical acidophilic character. These changes in the connective tissue are best studied in artificial tumors produced by the injection of certain dyes, and in beginning malignancies due to exposure to the X-rays. In these X-ray malignancies the depth of the invasion of the epithelium is coextensive with the changes in the connective tissue (Fig. 84). In this respect they exactly parallel the experimental epithelial hyperplasias. In both cases the loss of the acidophilic character of the connective tissue antedates the proliferation of the epithelium.

The primary structure of the skin may be retained for a considerable time. Pearl formation and the retention of the prickles may endure, even to the metastatic nodules. This is particularly true of those malignancies derived from long existing lesions. This is noted usually in the more slowly growing tumors developing from long existing hornified lesions. Usually, however, the tumor shows marked anaplasia early and the outlying growth, and particularly the metastases, have lost all semblance of the elemental epidermal cells.

Some expert pathologists (Broders, McCarthy) are able to determine the clinical character of the tumor from the cell forms alone. Such expertness in cytological judgment can hardly be expected on the part of surgeons. Fortunately, by considering the type of tumor and age of the patient together with the clinical history he supplements his histological judgment to such a degree that expertness in histology is less necessary.

Prickle cell cancers usually retain the alveolar form. Different cell forms, diffuse arrangement of cells with little connective tissue seen in epithelial malignancies elsewhere are seldom encountered in this type of tumor. Mitotic figures are observed in the more malignant types but may be absent. Degenerating nuclei are observed under certain conditions, usually after secondary infection has occurred.

Literature

To the student of today it seems impossible that there ever was a time when it was not known that carcinomas, as we know them today, were not the products of proliferating epithelium. Yet it was Thiersch (*Epithelialkrebs, Namentlich der Haut*, Leipzig, 1865) who demonstrated this fact in so far as it relates to the carcinomas of the skin. This is one of the outstanding contributions to tumor knowledge and is besides an outstanding example of how a scientific research should be pursued. Waldeyer (*Arch. f. Anat.*, 1867) extended this principle to include the malignancies derived from the mucous membranes. Prior to that time it was believed that carcinomas could be developed from connective tissue.

Skin malignancies, for clinical purposes, are generally divided into two groups: the basal celled carcinomas of Krompecher (*Der Basalzellenkrebs*, Fischer, Jena, 1903), and the prickle celled tumors of most authors—the acanthomas of Ewing (*Neoplastic Diseases*, Ed. 3, 1929, p. 862, Saunders), the flat cancers of Billroth (*Arch. klin. Chir.*, 1866, 7, 860; *allg. chir. Path. u. Therapie*, 1889, 908).

Thiersch (*idem.*) and Paget (*St. Bartholomews Hosp. Rep.*, 1874) had already divided skin malignancies into the superficial and deep. In many respects this concept is of more basic value to the surgeon than the modern classifications, for it emphasized the clinical differences.

More elaborate classifications have been proposed from time to time, notably by Unna (*Die Histopathologie der Hautkrankheiten*, Berlin, Hirschwald, 1894) and Hansemann (*Die mikr. Diagnose der bösart. Gesch.* Berlin, 1897) but such refinements confuse rather than aid the surgeon.

The student who wants to know everything about cancers must consult Wolf (*Die Krebskrankheit*, Jena, Fischer, 1907-1914).

Generally speaking, the more abundant the blood supply of a region the more malignant the tumor. The younger the patient, likewise the more malignant the tumor. The differences in malignancies find expression in differences in structure of

the tumor. This fact has been made use of by Broders (*Ann. Surg.*, 1921, 73, 141) who divides malignancies into four groups according to their cell type. This classification of the degrees of malignancy of tumors is of importance chiefly to the pathologist to whom the clinical data are not available. It requires a cytological understanding hardly to be expected of surgeons. Happily a careful consideration of the life history and location of the tumor anticipates the findings of the laboratory. The topographic location, the rate of onset and the age of the patient are equally as important as the histological findings.

Basal Celled Epitheliomas. Krompecher (*Zeigler's Beitrage*, 1900, 28, 1) is the outstanding work on the type of tumors developing from the seborrhoeic areas on the skin. Mallory (*Path. Histology*, Saunders, 1914, 373) is of the opinion that the basal celled tumors are derived from the hair shafts. This is particularly true in that type which form the long spindle type of cell. Some of these seem actually to be abortive attempts to produce hair. The importance of this fact has been much neglected. The more one studies the very early lesions the more important this becomes. Boormann (*Zeitschr. f. Krebsforschung*, 1904, ii, 1) believes the reticulated basal celled epitheliomas are derived from misplaced embryonal cell groups derived not only from the epidermis but from the skin appendages. This is obviously true of those which begin beneath the epidermis and independent of it, and involve the skin secondarily. This possibility should be kept in mind in the type which produces a reticulated or cystic structure. These sometimes begin under a silver-colored epidermis. Janeway's work (*Zeitschr. f. Krebsforschung*, 1910, 8, 403) has not received the attention it deserves. He has shown that these tumors may arise from basal cell inclusions in the skin. He has emphasized the changes in the connective tissue which are associated with and even precede the proliferation of the epithelium. These it may be noted are associated with the seborrhoeic lesions which precede the development of the tumors, sometimes by a considerable period of time. Bonney also (*Lancet*, 1908, i, 1389) has emphasized the changes in the connective tissue. This is interesting and sometimes antedates the development of actual cell proliferation in keratotic lesions and is sometimes most prominent at some distance from the tumor, apparently presaging the development of the malignancy and again it seems to be the result of the tumor growth. Here as elsewhere the connective tissue changes in epithelial malignancy have been too little regarded. The histochemical changes of the connective tissue are as important as those in the epithelium, and they begin first. Ewing (*ibid.*) describes the simple adenoid type of basal celled epithelioma, characterized by a circumscribed progressive tumor which may ulcerate and form metastases. It is the encouragement held forth in this paragraph that induced me to elevate this type to a separate group of tumors midway between the basal celled tumors and the acanthomas. This is more easily done in the clinic than in the laboratory and it is more important there.

Cheatle (*Brit. Jour. Surg.*, 1922, 9, 529) emphasizes the multicentric origin of basal cell epitheliomas not only from the epidermis but also from the hair follicles. Broders (*Jour. A. M. A.*, 1919, 72, 856) believes the basal celled tumors and squamous celled carcinomas are intimately associated in the same neoplasm and that the basal celled type may metamorphose into the squamous. This is a comforting viewpoint for the laboratory man but the clinician must individualize in these cases if he would avoid doing more than necessary in the simple cases and too little in the more malignant ones.

X-ray Cancers. Porter and White (*Ann. Surg.*, 1907, 46, 649) give in detail the progress of a patient suffering from this type of malignancy, setting forth not only the pathological findings but also the personal aspects of the disease. It has been my unhappy privilege to follow several such cases. The impressive factor is the multiplicity of pictures presented in the epithelial development and of degeneration on the part of the connective tissue. Adami (*Principles of Path.*, vol. ii, 1910, Lea and Febiger) believes that the first changes in X-ray malignancies are found in thrombosis of the vessels.

McNeal and Willis (*Jour. A. M. A.*, 1923, 80, 466) report a case of carcinoma following prolonged exposure to large quantities of radium.

CHAPTER IV

Fibrous Tumors of the Skin

A NUMBER of disassociated diseases may, for clinical convenience, be classified under this head. These include papillomas, the ubiquitous soft wart; the neurofibromas of v. Recklinghausen; and as a matter of convenience, the tumors of the nerve trunks; the neurolipomas; the subcutaneous lipomas; and without any particular reason, the keloids; and finally, because of a clinical resemblance to the neuromas, the myomas.

FIBROMAS

The dinky little soft warts are usually treated with contempt by surgeons, seldom being regarded as of sufficient importance even to be sent to the laboratory. Yet they lie at the threshold of a large, intensely interesting complexity of tumors, presumably of neurogenic origin, for the most part beyond the comprehension of the surgical pathologist. Until pathologists are able to define more clearly the various groups of tumors now believed to be of nerve origin it is best to stick to the old convenient clinical classification and to arrange histological studies about such groups. To treat logically now all the tumors that are now believed to be related in genesis to some nerve elements would be to bring together tumors clinically insignificant and those distinctly malignant. While a clinical classification leads to certain artificial divisions from the scientific standpoint the practical convenience of so doing is great.

Hence it is convenient to classify the fibromas of the skin into the simple fibromas and the neurofibromas though one cannot know when an apparently simple fibroma will become a neurofibroma. Apparently simple fibromas may multiply until a typical v. Recklinghausen's disease has formed. Unfortunately the consideration of the neurofibromas leads us, without a chance for logical separation, to the more deeply lying tumors of nerve origin so that this chapter includes growths ranging from the simple wart to the sarcomas of the nerve sheaths.

Evidence is accumulating which tends to show that even the various forms of melanomas have their genesis in disturbances in nerve development. Yet because of their great clinical importance these are best treated as a separate group for they have life histories all their own.

Papillary Fibromas. Under this head may be included that variegated group of tumors, which occur most commonly on the trunk, and are characterized by their soft structure and sessilated or pedunculated form. The surface is often bosselated. There is no sharp dividing line between them and certain melanomas on the one hand and the neurofibromas on the other. This fact is particularly worthy of emphasis since atypical and not yet fully developed forms of v. Recklinghausen's disease begin

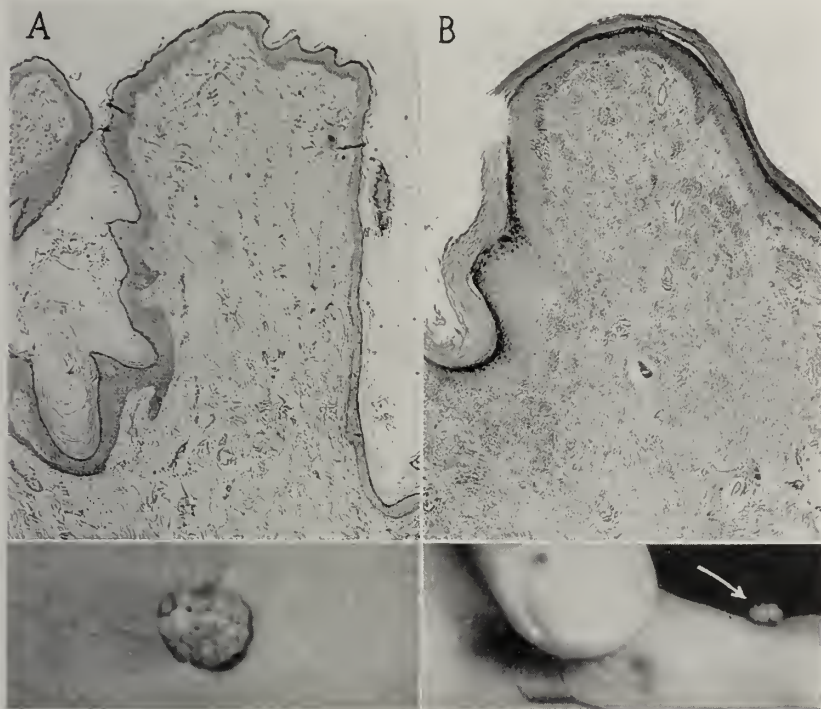


FIG. 85. Soft fibromas of the skin. *A.* Composed of loose connective tissue with few cells and covered with a uniform layer of epithelium. *Insert*, tumor natural size showing lobulated surface. *B.* Composed of fibrous tissue which contains many nevoid-like cells. *Insert*, tumor natural size.

apparently as multiple soft warts. The soft fibromas are a tricky sort; though usually devoid of nevoid cells some of them contain them. Those which contain the nevoid cells not uncommonly become malignant. In this type irritation, such as ligating their bases, may start them off on a career of destruction. Such warts, of course, should be classified as amelanotic melanomas but they are clinically indistinguishable from the pigment-free papillomas. Therefore soft pedicled warts should always be regarded with suspicion, particularly when they occur in old persons.

Pathogenesis. Papillary fibromas are seen most commonly in persons at or past middle life. They begin as barely perceptible soft protuberances and in the course of years attain their characteristic form (Fig. 85). They may attain a considerable size even as large as a fist but usually they remain small, hazel or hickory nut size. Their attachment to the skin may be by a narrow pedicle, so small in fact that they become detached during the ordinary vicissitudes of life.

As a corollary may be mentioned a rarer form which begin as small inflammatory lesions, undergoing a stage characterizing the granuloma pyogenicum, acquiring an epithelial covering and by the process of productive reaction attain the dignity of a neoplastic process. While undergoing such changes the cellular element, because of the abundance and size and the close association with the blood vessels, may lead the unwary into diagnosing sarcoma. Such tumors, it may safely be said, are not of neurogenic origin.

Pathology. Softness is the characteristic of fibrous papillomas but occasionally when the fibrous tissue is abundant they may be quite firm. They are of the color of the surrounding skin. When yellowish in color the epidermis may be unusually thin and the fat content abundant but likewise it may mean that there are amelanotic nevoid cells beneath, always a dangerous complication. When cut across a piriform yellowish mass covered by a thin uniform skin is apparent. The color varies with the proportionate admixture of fatty and fibrous tissue.

Histology. The microscopic picture is confirmatory of the gross section. Sometimes the entire tumor is made up of loosely arranged connective tissue with sparse ovoid cells (*A*, Fig. 85). Others consist of numerous connective tissue cells which differ from fixed tissue cells only in their size and relative number. The denser varieties, particularly those developing from infected or other reactive areas, may show little other than strands of fibrous tissue. Their relation to keloids may in their early history be quite close.

Others, while they are covered by a thin skin as with the preceding, have in addition clusters of amelanotic nevoid cells (*B*, Fig. 85). Later they may acquire pigment. This is the type which when irritated, as by tying a string about the base, may become malignant. This shows the relationship to the melanotic warts which is further emphasized by the fact that the metastases may contain pigment.

The fibrils may be fine or large resembling keloids. They may imitate embryonal connective tissue, sometimes almost mucoid, approaching the structure of fibroma mollusca; indeed there is no sharply defined line microscopically as there is none grossly.

The blood vessels may be abundant but there is no need of complicating the picture by the use of the term "angiofibroma" sometimes used to designate them. The blood spaces exist at the whims of the connective tissue and take no part in the life history of the tumor.

Lymph spaces may be so prominent, and the resemblance to elephantiasis so close, that from the microscopic picture alone, a classification could not be made. These resemble in structure the huge fibroma molusca.

Cutaneous Fibromas. These fibromas are uniformly firmer than the preceding, thereby justifying the term. They may lie within the skin or form protuberances above it.



FIG. 86. Hard tumor in palm of hand. F., age 16. No symptoms. *Insert*, dense fibrous tissue with sparse spindle-form nuclei.

Pathogenesis. Slow of onset they may first attract attention by the formation of firm nodules within the skin (*Insert*, Fig. 87), or they may gradually form rounded firm protruding tumors. These tumors may cause indefinite pain thereby suggesting a close relationship with neurogenic tumors. In fact there seems to be no dividing line between the two. This is particularly true of those that remain intracutaneous, time being a more accurate determining factor than microscopic examination. The protruding form (Fig. 86) are more definitely fibrous and may exist many years without change. The most common location of the protruding form is in the palms of the hands while the intracutaneous form are most commonly found in the forearms and legs.

Pathology. The intracutaneous form (*Insert*, Fig. 87) occur as hard areas set within the skin without any sign of encapsulation. It is this fact that makes their neurogenic origin probable and their clinical disposition questionable. The protuberant form are more dense and are usually more definitely encapsulated but not to the degree that they can be shelled out. These resemble in form the so-called transplantation dermoids commonly seen on the palmar surface of the hands and quite possibly have a similar genesis.

Histology. The intracutaneous form are made up of whorls of fibrous tissue intimately associated with the skin. The relation of the fibre bun-

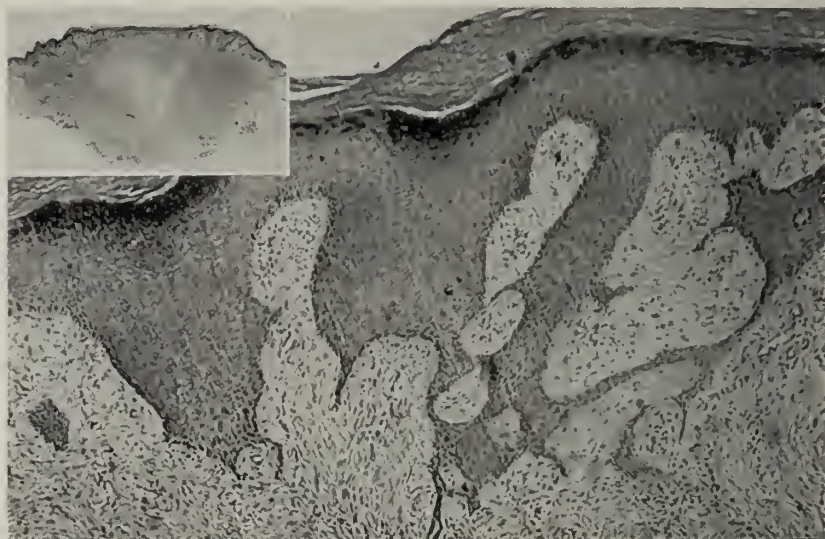


FIG. 87. Intracutaneous fibroma, likely of neurogenic origin. The bulk of the tumor is made up of whorls of dense fibrous tissue. The covering epidermis shows marked hyperplasia. *Insert*, gross section, natural size. The tumor shades gradually into the surrounding tissue.

dles suggests a nerve derivation (Fig. 87). At any rate, the tendency now seems to be that when in doubt, call any tumor neurogenic and be safe from criticism. The globular form are made up of dense fibrous tissue with sparse spindleform cells (*Insert*, Fig. 86).

LIPOMAS

The ubiquitous fatty tumors are nearly always wholly benign and they usually become of clinical interest because of their size. However, they bear certain relationship to other conditions notably the neuromas

which are of great clinical interest. The deeper forms may be related to the myxomas, and hence to the sarcomas.

Pathogenesis. Lipomas usually begin as globular tumors beneath the skin and as they grow they lift the skin over their summits. The back, shoulder (Fig. 88) and abdomen are the common habitats, but no region, not even the palms or the soles are entirely immune. Formerly these tumors were sometimes allowed to attain a huge size; I once removed one weighing 15 pounds. But usually there is an anxious surgeon



FIG. 88. Lipomas of shoulder. *A.* M., age 60. Soft tumor of back. Many complicating interdigitations made removal difficult. *B.* M., age 56. Soft ovoid tumor over front of shoulder. Shelled out easily.

to greet them as soon as they attain an appreciable size. Patients frequently accuse them as the causative factors of obscure pain (Fig. 89). In such cases if the surgeon accepts the patient's opinion removal causes disappointment.

Sometimes the covering skin becomes thinned, particularly in those containing a considerable admixture of fibrous tissue. These suggest a relationship to certain fibrosarcomas of the skin. Sometimes they form overhanging masses suggestive of fibroma molluscum (Fig. 89). The close relationship between the lipomas and the neurogenic tumors is shown by the occurrence of multiple lipomas along the course of cutaneous nerves

(Fig. 90). These are commonly symmetrical and occur most commonly on the arms but are not uncommon on the trunk. They seldom cause pain but may do so. They do not attain a large size. They are possibly related to Dercum's disease.

Lipomas usually have a chief supplying vessel from which branches go to the various lobules. This arrangement is the common one even in



FIG. 89. Pendulous lipoma. M., age 37. Came in because of sciatica. Large soft, overhanging tumor with no clinical symptoms. Has been present since infancy.

the large and complicated tumors. Sometimes lesser independent vessels supply individual lobules.

Pathology. Lipomas are soft even semi-fluctuating to the feel and are usually globular and encapsulated. Prolongations extending into the surrounding subcutaneous tissue (Fig. 91) often complicates their removal. Failure to remove the interdigitation may lead to the development of new tumors. The multiple cutaneous lipomas are less completely encapsulated and while undoubtedly associated with the nerves this can seldom be demonstrated at operation. In fact there is no excuse for their removal except curiosity on the part of the possessor or possessee. On cross sec-

tion lipomas are uniformly yellow in color except in the firmer forms which may be interrupted by fibrous bands. Myxoid admixture is made manifest by light pinkish semitranslucent areas.

Lipomas sometimes undergo a variety of degenerative changes. Liquefaction and calcification are the most common. In certain situations, as in the region of the abductor group of muscles, they are prone to have myxoid areas which in turn may harbor sarcomatous degeneration. Just what the genetic relationship of these various tissues may be is a matter of speculation.



FIG. 90. Symmetrical lipo neuromas of the forearm. The skin was freely movable over some of the tumors but in some there was a more or less intimate attachment. They caused no symptoms.

Histology. Aside from the fibromas and the neuro-lipo-fibromas these tumors are made up of typical lipid cells. Sometimes some areas show vacuolation causing a xanthoma-like appearance. The fibrous tissue admixture may be so great as to warrant the term "lipo-fibroma." Even more important is the myxomatous admixture. Sarcomatous areas are often found where myxoid areas are common.

NEUROMAS

There is a general tendency to widen the field of tumors derived from nerve tissues. Masson particularly has extended our knowledge of the relation of nerve endings to tumors not previously suspected of such relationship. These researches promise to become of enormous

practical value but at the present time some of the recent advances are not sufficiently proven to warrant their acceptance by the surgeon. Some of these problems therefore may, for the present, be left in the hands of the pathologists.

Numerous skin tumors, including the melanomas and fascial tumors and the like, are being now included by many authors with the neurogenic



FIG. 91. Lobulated lipoma from the shoulder. It shows the lobulations which interdigitate into pockets in the surrounding tissues.

tumors, apparently with good reason. However, for such tumors as have a well established pathological anatomy, and in which the clinical course is well known, it is best to retain the well established terms.

Therefore only those tumors in which a relationship to the nerves has been certainly established and which have a definite life history need concern us here.

Most nerve tumors spring from the connective tissue of the nerves

and are not really neuromas, hence the term "false neuromas" has been applied. This term means of course that they are not neuromas at all. A better term is "neurofibromas," indicating that they are derived from the fibrous elements of nerves. To me, I am free to confess, this group includes those things which by common consent are accepted as neurogenic, though they bring to me no self-acquired anatomic picture. In making



FIG. 92. v. Recklinghausen's disease. M., age 54. Numerous soft elastic nodules covering chest and back. Present many years. Patient had neuroblastoma in the cervical region which was removed. Died later of recurrence.

this confession it is comforting to note even our ablest histologists, when writing on this subject, use borrowed cuts from old authors indicating that histological proof is difficult to produce else they would publish pictures of their own making. One may cover this group best perhaps by calling them, with Ewing, "cutaneous neurofibromas." Only tumors which contain new formed nerve elements should be called neuromas. In contradistinction to the preceding they are called "true neuromas."

Since, however, the whole matter is yet so involved in controversy I shall designate them tumors of the nerve trunks, thus avoiding the necessity of taking sides in a controversy much of which is beyond my ken. Ewing calls these deeper neurofibromas.

Cutaneous Neurofibromas (v. Recklinghausen's Disease, Fibroma Molluscum). These tumors are found within the skin or extending above it. Clinically they form something of a motley group. It seems a far cry



FIG. 93. Fibroma molluscum. M., age 59. Entire body covered with tumors varying in size from a pea to a hen's egg. The skin of the forehead is made firm and elastic by the close arrangement of the tumors.

from the single pea-size nodule within the skin or projecting above it to huge pedunculated masses (fibroma molluscum) or the countless nodules, limited only by the available area to give them place (v. Recklinghausen's disease).

Pathogenesis. In the simpler forms they appear in early childhood as soft fibrous warts, slightly elevated above the surface of the skin, varying in size from a pea-size to that of a hickory nut (Fig. 92). But they may be

much larger, even pedunculated or pendent. Usually the tumors are soft, easily lifted up and stretched out like little nipples. As they grow larger they may become pedunculated, even sessile. They cause no disturbance except by their presence. To this type the eponym, *v. Recklinghausen's disease*, is applicable. The hard form which develop within



FIG. 94. Fibroma molluscum. F., age 59. Mass growing from side of neck for many years. Rapid growth past few months. Many small brownish spots and nodules scattered over body. Tumors removed by Dr. Frick. Prompt recurrence with metastases in lungs.

the skin produce a nodulated firm skin so that a whole area moves en masse (Fig. 93). The pendulous form may become much more than mere annoyances. Rarely they hang down as enormous masses (Fig. 94) forming serious handicaps to the patient's activities. This type is most common in the temple and neck, and about the hips, and are generally soli-

tary though they may be multiple. This form deserves the term "fibroma molluscum."

Many of the smaller and solitary tumors are associated with an increase in pigment. This is of interest as it suggests a relationship of all pigmented tumors to developmental disturbances in the nerve endings. Those possessed of a penchant for speculation may find a diversion in tracing the various cell types in malignant melanomas to the various cell forms in developing nerve endings.

But it is not mere speculation to associate these tumors with malignant degeneration. Sarcomas may develop in them or in the scars remaining after their removal. In fact it has been estimated that some eight per cent ultimately destroy life by extension of the tumors. These often obliterate the line between the dermal and subdermal varieties. Furthermore some of these innocent tumors are associated with bone changes, such as deformities and abnormal growths, and with cysts or pedunculated tumors beneath the periosteum or cysts within the medulla of the bone. Once started on this track the possible relation to other bone diseases of obscure nature to the nerves must be considered.

There is no sharply defined line between the cutaneous form, *v.* Recklinghausen's disease, and the more deeply lying, the so-called cirroid neuroma, the fibroma molluscum. The latter produce bulky ill-defined masses in which the cord-like nerve trunks may be palpated. These are also called plexiform or cirroid neurofibromas. This is the type which is most prone to undergo malignant change. They extend into the deeper structures, even to the bones, so that operation is not feasible, often impossible. A prompt return is the rule and malignant degeneration seems to be hurried by operative treatment. This form usually occurs elsewhere than on an extremity and even when so located amputation is impotent to stay the progress of the disease, due to extension rather than metastasis. This form of neurofibromatosis resembles certain forms of elephantiasis; possibly there is not always a definite division between the two.

The ubiquitous amputation neuromas, which occur at the ends of nerves after amputation, hardly deserve to be classified as tumors. They are more nearly analogous to hypertrophied scars and are due to increase of fibrous tissue and of nerve elements in their futile attempts to reunite with the part which has been amputated. Aside from the pain they cause they are clinically innocent. When removed and a proper plastic operation is performed in healthy nerve tissue the chapter is ended.

Pathology. The small tumors of *v.* Recklinghausen's disease are soft and elastic but some are fairly firm. The larger ones flap about when

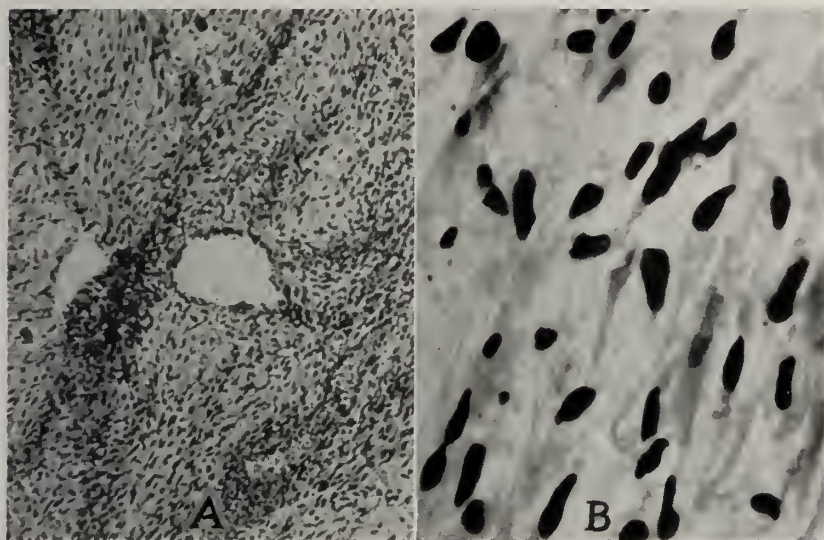


FIG. 95. Fibroma molluscum. *A*. Cellular area at base of tumor. There are many short spindle cells in a homogeneous palely staining connective tissue. These cells are intimately associated with the vessel walls. *B*. High power shows the cells to be irregular in shape and size. Their nuclei stain deeply but not uniformly.

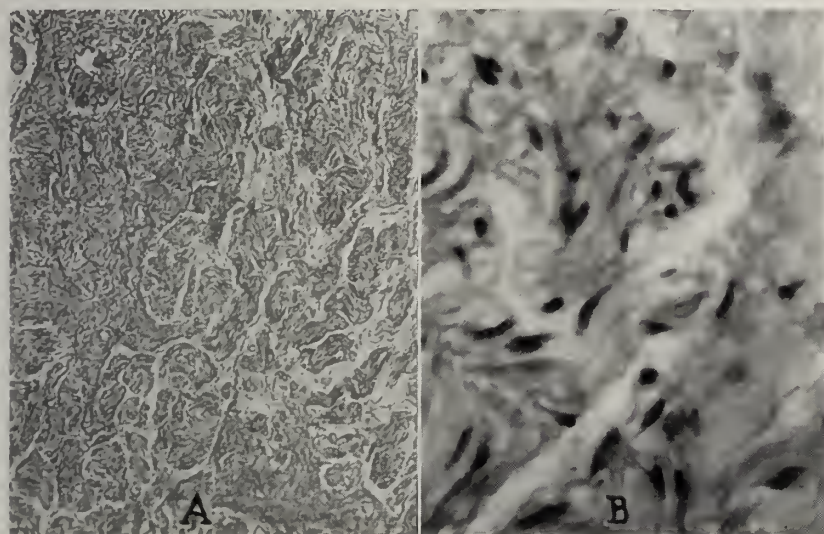


FIG. 96. Slide of amputation neuroma. *A*. Whorls of nerve fibres forming interlacing bundles between which are connective tissue fibres with the form and staining characteristics of keloid. *B*. High power of same showing the general spindleform character of the deeply staining cells.

manipulated. They give the sensation of being loosely attached to the skin though some are definitely incorporated in it. When hard nodules occur, particularly when the dense area is situated near the base of the tumor malignancy must be suspected. Section but confirms the gross palpation. The cut surface is white, glary, semi-translucent in spots. The knife rolls the tissue before cutting it. Often fine strands traverse the tumor and in the denser forms well defined intertwining bundles may be made out. If the tumor is hard and the surface homogeneous and pinkish beginning malignancy is probable.

In the cirroid neurofibromas the nerve bundles are easily identified by sight and touch suggesting in gross outline cirroid aneurysms. The cut surface is glary, almost mucinous, indistinguishable from some types of elephantiasis due to lymphatic occlusion.

Histology. The impression of interlacing fibres observed on gross section is confirmed by the slide. Between these are tumor cells, spheroidal in the soft, spindle-form in the firmer types. In the denser types the cells may be very sparse. Whether these cells are derived from the nerve tissue or not does not appear to be established. When they are numerous and intimately associated with vessels the possibility of malignancy must be suspected (*A*, Fig. 95). Large or spheroidal deeply staining cells particularly should cause apprehension (*B*, Fig. 95). This suspicion is confirmed by the local recurrence and the formation of metastases. Until this happens one cannot be sure of the histological diagnosis but it helps some to suspect this eventuality.

The false (amputation) neuromas are made up of wavy fibre bundles (*A*, Fig. 96) between which are elongated densely staining cells (*B*, Fig. 96).

Tumors of the Nerve Trunks. Under this heading one must consider tumors involving the nerve shafts as well as those developing from terminal nerve elements. The controversy long waged whether or not nerve tissue is capable of producing tumors seems gradually to be acquiring an affirmative note. Nevertheless the surgeon must have a mental picture of those tumors which obviously involve the nerve shafts but which show no nerve elements. To his conception he may add the broader group in which no nerves can be demonstrated but which are accepted as neurogenic largely on the grounds of histological analogy. Much more common than tumors of nerve elements are the cutaneous or subcutaneous nodules which can be demonstrated as involving a nerve trunk going out from some of the connective tissue elements. This is made up of spindle cells and much connective tissue but other forms such as xanthomatous, myxoid or sarcoma formation are quite common. These have all the ear-

marks of such tumors developed from whatever source and since it is these elements that play the larger part in determining their course, they should have a prominent place in the terminology, such as neurosarcoma, or perhaps better still, sarcomas of the nerve sheaths.

Even deep nodules formerly not suspected as of neurogenic relationship are now known to have such. These may be in the retroperitoneal or other deeply lying nerves and even in the nerves of viscera. All these possibilities make of the deep neuromas a difficult problem.

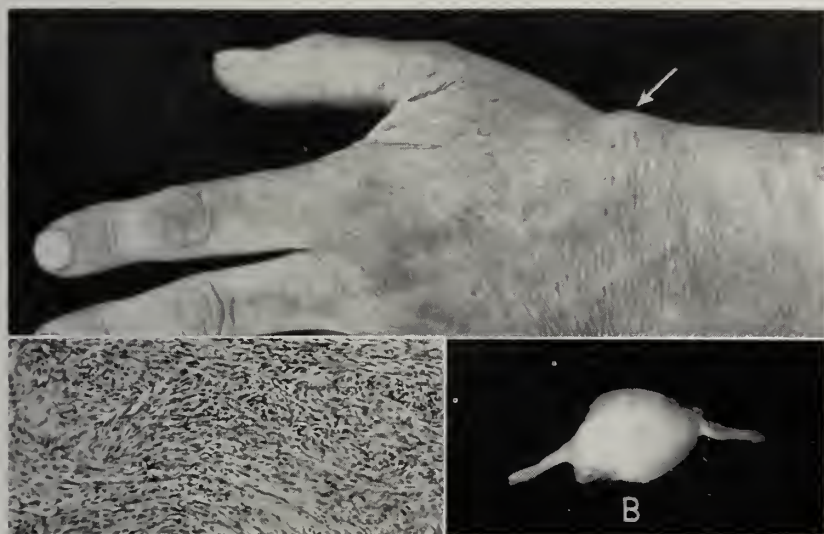


FIG. 97. Neurofibroma of a cutaneous nerve. M., age 48. Painful tumor on top of wrist several years. *A*, Fibrocellular structure; *B*, gross appearance, natural size.

Pathogenesis. Neurofibromas of the nerve trunks in their simplest form occur as subcutaneous spheroidal tumors which elevate the skin and are easily seen on simple inspection (Fig. 97). They are firm to the touch, movable under the skin, indicating a more or less complete encapsulation. Clinical experience confirms this for usually simple excision eliminates them. Usually the nerve trunk can be demonstrated at operation as it enters and leaves the tumor (*Insert*, Fig. 97). These tumors involving large trunks, most commonly the sciatic, may attain a large size and yet not interfere with the function of the nerve. They are clearly of the nerve sheath for early the nerve trunk can be separated from them. Later on the nerve bundles interdigitate with tumor structure making separation hopeless. When the tumors affect important nerves such as the sciatic, a resection of the entire nerve trunk is anatomically unper-

missible since a useless leg is inevitable and even with amputation derivative central metastases too often greet the surgeon's efforts.

The pestiferous hard little nodules which occur in the skin must belong to this group for they tend persistently to recur (Fig. 98). They differ from that sub-group of melanomas, which I have called chromomas, in that they are painful, do not tend to ulcerate but recur as subdermal or at least subepithelial nodules, gradually widening their scope until a state of inoperability is reached. In this they bear a relationship to the spindle cell type of melanomas but they never produce pigment, either in the primary tumors or in the metastases.



FIG. 98. Neuroma of arm. M., age 42. Growth in forearm for 25 years. Painful last 3 or 4 years. Tumor movable latterly only. No recurrence after five years. Insert, shows cellular structure.

Those neuromas which lie more deeply are attached to the fascia and are immovable except as they roll with the movement of the deeply lying soft parts. There is a general tendency now to class such tumors as neurogenic, without, it seems to me, adequate evidence. For this reason I have chosen to discuss them with the fascial tumors, for it is as such that the surgeon has to deal, for his troubles are topographic and fine points of genesis concern him but little. They grow larger than tumors of demonstrated nerve origin and may produce bulging tumors of considerable magnitude. At operation no nerve trunk can be demonstrated. They seem everywhere to be attached to the fascia and the tendency to local recurrence confirms this. Usually each recurrence shows an increased cellularity expressed by wider and wider attachment until blood

vessels, large nerve trunks and even the periosteum are involved demanding amputation, made futile too often by metastasis in the mediastinum or lungs, seldom in other viscera.

Often elemental tissue tumors such as lipomas, myxomas and particularly myxosarcomas are associated with the larger nerve trunks, notably the sciatic. There is no evidence that any of the essential nerve elements take any part in the production of these tumors.

Pathology. Neurofibromas are firm elastic to the touch; their semi-fixation when attached to the subcutaneous or intermuscular fascia is

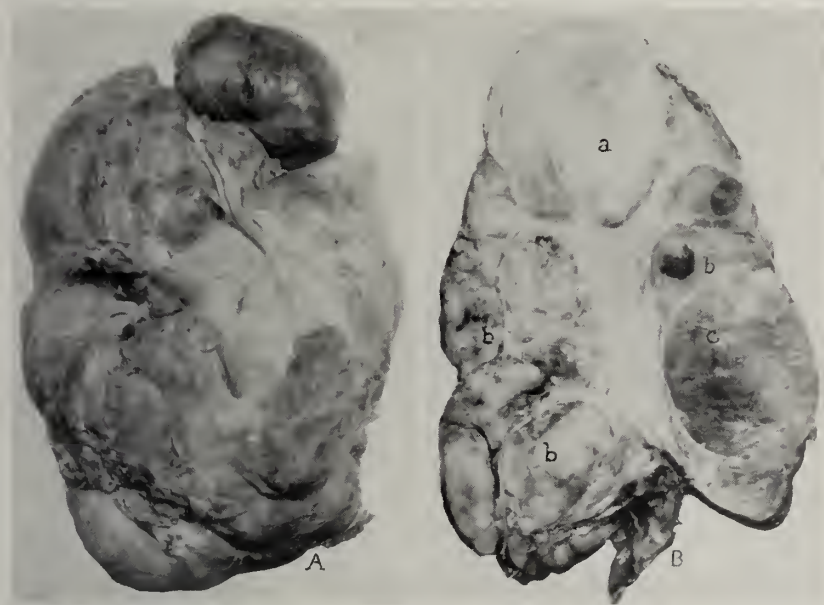


FIG. 99. Myxosarcoma of the sciatic nerve. F., age 32. First noticed a tumor behind and above left knee 10 years ago. It has grown rapidly in the past 3 months. Moved latterly only. Removed. Chest metastases 4 months after operation. A. Gross specimen, irregular, lobulated, 4 x 6 inches. B. Section of same: a, soft translucent area of pure myxoma; b, b, pale pink myxosarcoma; c, darker area of small and spindle celled sarcoma.

always in evidence. The cut surface is firm white glistening, generally homogeneous, without evident fibre bundles. This description holds for those obviously attached to cutaneous nerves. Those more deeply situated have much the same appearance save a nerve origin is not demonstrable and they tend more persistently to recur.

Bundles of preserved nerve fibres often can be demonstrated at the operating table in large tumors of the deeper nerves, myxoid, fibrous,



FIG. 100. Slide of neuroma of peroneal nerve: *a*, nerve fibres; *b*, connective tissue bundles with round cells. Without specific stains neuromas cannot be positively identified with ordinary stains. It is the dense whorl-like arrangement which suggests a neural origin, the clinical evidence must provide supporting evidence.

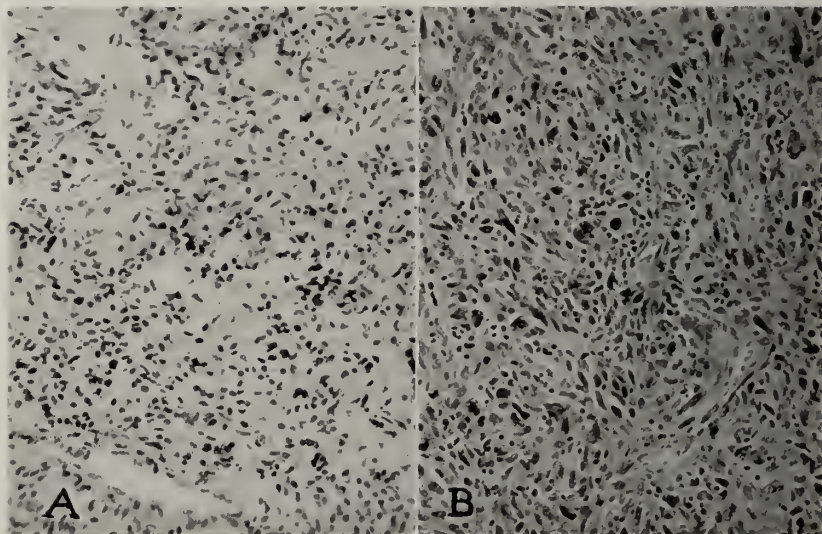


FIG. 101. Slide of recurring neuroma of arm. The primary tumor was not available but that removed at the first recurrence. *A*, was made up of fibrous tissue with numerous short spindleform cells. *B*. Tissue removed at the fourth recurrence. The cells are numerous, irregular in shape and size and all stain deeply.

sarcomatous, as the case may be (Fig. 99). These are clearly specific tumors and their association with the nerve is incidental. The surgeon should not allow new theories of origin to disturb his well earned knowledge of the life of the tumor.

Histology. The structure of the harder forms is that of a dense fibroma (Fig. 100). Sometimes they are more cellular (Fig. 101). Malignancy should then be suspected. Often the fibrous character belies their malignant character and it is only when one knows their source that their clinical importance is evident. In fact, so commonly are these tumors

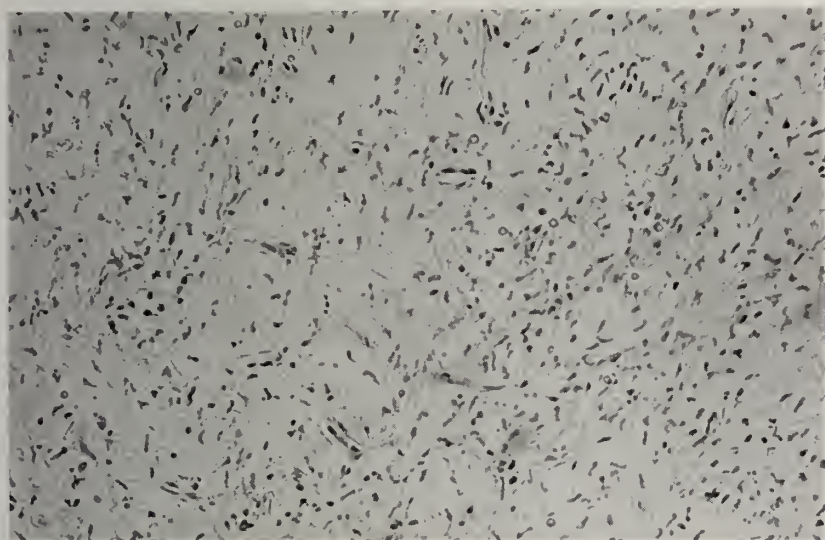


FIG. 102. Slide of myxosarcoma of the sciatic nerve. Spindle and stellate cells are imbedded in a myxoid matrix.

malignant that a benign tumor should not be diagnosticated from the microscopic picture alone. The more rapidly growing are often more cellular, even losing their distinctive fibrous character. The tumors of the large nerves may show xanthomatous, myxoid, as well as fibrous areas and often nerve bundles which the tumors have incorporated in their process of development (Fig. 102). It is the association of these tumors rather than the histology that gives the clue to their nature.

Neuromas of Sympathetic Nerves. Tumors associated with the sympathetic nerve trunks are likely to be multiple. Their identity may be suspected when obscure tumors are encountered corresponding in topography to that of the sympathetic nerve trunks and away from the usual site of lymph glands.

Pathogenesis. Because of their deep situation they are not detected until they have formed tumors of some size. They are usually ovoid but may be spindleform particularly when multiple (Fig. 103).

Pathology. In hand they are soft like a Hodgkin's gland from which they must be distinguished but they are generally larger, often spindle-form or with a pointed end. The cut surface is white, homogeneous but uniform and never shows degeneration.



FIG. 103. Retroperitoneal neurofibromas. M., age 22. Patient has had dull pain in the left side for several years. Sudden movement or jar causes acute pain. Noticed a mass in the side one month ago. Operation showed a series of ovoid, yellowish elastic tumors extending from the diaphragm to Scarpa's triangle. Free from recurrence after 10 years. (Tumors reduced two-thirds in the cut.)

Histology. These tumors are made up of bundles of fibrils (*A*, Fig. 104); the chief characteristic is the interspersed small cells with intensely staining nuclei (*B*, Fig. 104).

KELOIDS

Two forms were formerly recognized, the true, arising spontaneously without a previous injury and the false developing in a scar. The structure is identical and this division is now generally abandoned.

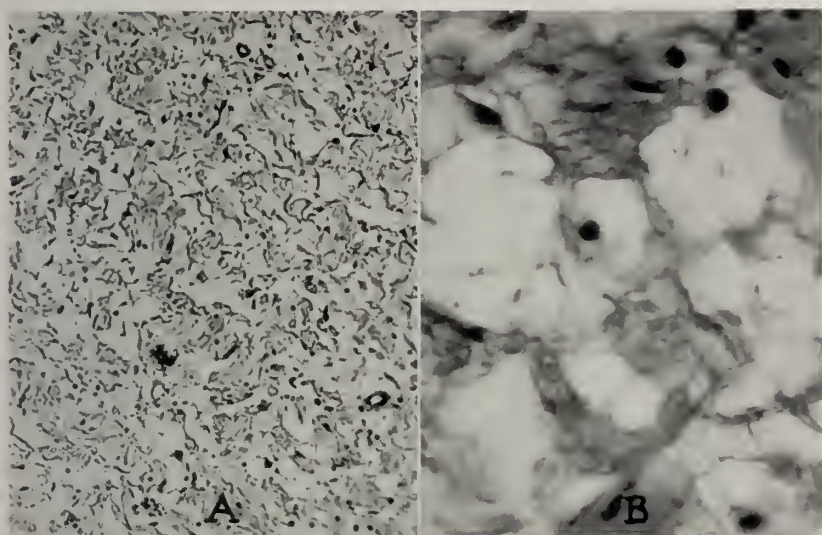


FIG. 104. Fibroma of sympathetic nerves. *A*. Low power showing interlacing fibrous tissue. The interstices between the connective tissue bundles are filled with a myxoid tissue. *B*. High power of the same shows these areas quite free from stain. The cells are very sparse, the nuclei round and deeply staining.

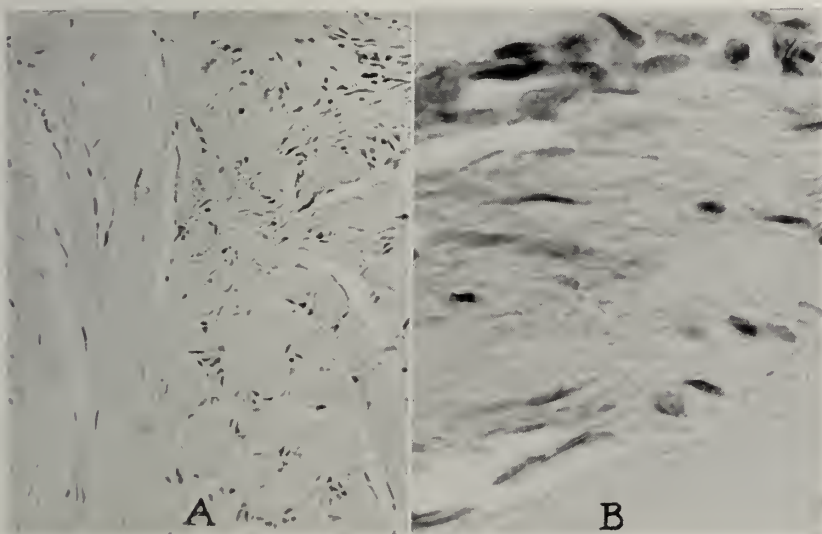


FIG. 105. Keloid from a scar over the sternum. *A*, heavy bundles of fibres are shown running vertically at the left of the picture while on the right their great size is shown by the cross-sections. *B*, in the lower part of the cut the nuclei are small spindleform, while above they are larger and deeply staining.

Pathogenesis. The onset is insidious, usually in a scar, the first appearance presenting a roundish dome-shaped elevation, red in color and firm to the touch. Sometimes they take the form of the scar in which they develop but quite as often but a part of the scar is involved in the growth. They most commonly develop in the scars after burns and in the negro race. When they develop independently of scars they are often multiple.



FIG. 106. Myoma of the skin. F., age 45. Tumor followed injury from a thistle. Nodule the size of a hickory nut noticed first 6 years ago, involving the skin. *Insert*, interlacing bundles of nonstriated muscle fibres.

A keloid-like hypertrophy often occurs in scars, particularly in those which follow burns, which later regress. Such states are best called hypertrophied scars, though it cannot be foretold in the individual case whether or not it will regress. It is common to see a part of an incision become hypertrophic while the remainder of it runs the normal course. Time only distinguishes them from keloids. There is nothing the surgeon does or leaves undone which accounts for their development, a point of comfort if not of protection from legal persecution.

The important clinical fact is that keloids when removed tend to return if removed by operation. Keloids are usually symptomless causing annoyance only from their size. Sometimes they cause pain and it is said they may ulcerate and even take on malignant change.

Pathology. Keloids are firm almost cartilaginous to the touch and they give the same impression to the knife when cut, only they offer more resistance. They are usually pale red in color and their fibrous structure is usually apparent to the naked eye.

Histology. Keloids are made up of heavy bundles of fibrous tissue (*A*, Fig. 105). These bundles run more or less parallel but may interdigitate. The nuclei are sparse spindleform and commonly faintly staining. In some areas, particularly in the growing ones larger and more deeply staining nuclei may be seen (*B*, Fig. 105).

MYOMAS

Tumors springing from the nonstriated fibres of the errectores pilorum are rare. Some authors recognize a second class supposedly springing from the walls of vessels. Really they belong to one group, springing from we do not know where.

Pathogenesis. These are rare tumors varying from pinhead to walnut in size. They may be single or multiple. They may develop in the skin, where they resemble fibromas, or beneath it elevating the normal or attenuated skin above them (Fig. 106). They are always benign. They sometimes cause pain after the patient accidentally finds them, and they seem to cause dermatologists some pain.

Pathology. They are not truly encapsulated but are well circumscribed. On section they are of a uniform deep brown in color.

Histology. These tumors are made up of whorls of nonstriated muscle fibres. A resort to tinctorial chemistry is sometimes necessary to distinguish them from fibromas (Fig. 106).

Literature

Neurofibromas. A study of the literature impresses one with the vast possibilities the study of this subject encompasses. As might be suspected from the eponym "v. Recklinghausen's disease," it was that distinguished pathologist who first definitely established the relationship between long recognized soft multiple skin fibromas and the nerve trunks.

The relationship of the nerve trunks to lesions heretofore not suspected as being of neurogenic origin forms a promising chapter for the young surgeon. Ludy (*Arch. Dermat. and Syph.*, 1930, 21, 419) suggests a relationship of the nerves with nodular lesions of the skin which suggests a relationship with what I have called "chromomas" (*Annals Surg.*, 1928, 87, 99).

Incomplete forms of v. Recklinghausen's disease have been discussed by Wise and Eller (*Jour. A. M. A.*, 1926, 86, 86). Such studies are important because they make clear the relation of certain pigmented spots which afterwards form nonmalignant nodules to the nervous system. Because these areas are pigmented we are again reminded of the possible relationship of all melanotic tumors to the nerve endings.

Recently the involvement of the bones in v. Recklinghausen's disease has been recognized. Brooks and Lehman (*Surg. Gynec. and Obst.*, 1924, 38, 587) have reviewed this phase of the problem and have added important observations. This starts us anew on the road to speculation as to the possible relationship of other obscure bone lesions to the nervous system, and makes one wonder if there will not soon be Recklinghausen specialists or even Recklinghausen wards in our psychopathic hospitals.

Masson (*Ann. d'Anat. pathol.*, 1926, 3, 417; *ab. Cancer Rev.* 1926, 1, 482) has produced an outstanding contribution to the neurogenic origin of a variety of tumors.

Cohn (*Arch. Surg.*, July 1928, 17, 117) in a very able paper brings up the problem of the epithelial origin of certain nerve neoplasms. This paper again brings up the possible relationship of such tumors and certain types of melanomas.

CHAPTER V

Melanomas

THIS term designates tumors containing a specific pigment, the melanin. They vary in size from barely visible colored points in the skin to tumors of considerable volume. They may be congenital or may not appear until later life. They may lose their pigment and disappear but still remain potent sources of mischief. They range clinically from perfectly innocent spots to the most malignant of tumors. These habits, together with our ignorance of the source of the pigment, render this tumor, as Ewing states, one of the most notable topics in oncology. Whether they shall be regarded as epithelial in origin, therefore carcinomas, or of connective tissue derivation which would class them with the sarcomas, is immaterial. That both classes are represented is probable. Be this as it may they form a class of tumors with peculiarities all their own, comparable neither to the carcinomas nor sarcomas. This has not impressed the pathologist as much as it has the surgeon who knows from clinical experience that they are something quite apart from both the epitheliomas and sarcomas. Hence clarity will be enhanced by calling them melanomas.

They have their origin in groups of undifferentiated cells found beneath the epithelium, usually called nevus cells—that is mole cells. Simplicity will be fostered by thinking of them only as embryonal cells, as Senn called them, for they never produce a tissue warranting the use of any term suggesting maturity. If these cells are of epidermal origin the separation occurs at such an early date that they never attain the biological characters of epidermal cells. Possibly some of them eventually will be determined to be of neuroblastic origin. This is particularly likely of those tumors which develop below the epidermis and destroy it secondarily.

The problem of the melanomas represents nicely the surgeon's relations to pathology in general. If he, either before or after its removal from the patient, is able to recognize the tissue in hand and can deduce the subsequent course of the disease and can foretell what the slide will show in the laboratory he has all the knowledge necessary for his work. To him the whole vast literature of the nature and genesis of the melanin-producing and -bearing cells is beside the question. Algebraic symbols would be quite as useful as the terms now employed. If he can clarify

his clinical problems by making subdivisions, either on a morphological or clinical basis, he is justified in doing so even though the fundamental anatomic factors remain obscure.

The diversity of their growth possibilities is well shown by the rate of growth of tumors which they produce. The small pigmented warts giving rise to diffuse cellular tumors which cause death in a few months are contrasted sharply with the fibrosing type which drag on for years. Clinical observations lead me to suspect that perhaps Virchow was right, in a measure, in dividing melanomas into two groups, those derived from epithelial cells and those derived from connective tissue. But to say "derived from" prejudices too much. It were better to say the one tended toward development into epithelial, the other into connective tissue. The truth is, melanomas are never epithelial and never connective tissue in origin. They are the derivatives of embryonal rests and remain outlaws throughout life. One can only say some tend to remain spheroidal celled whether benign or malignant while the others tend to develop connective tissue. The two types find expression in their clinical course and I believe they run equally true to form in the laboratory. Adequately descriptive designations are lacking. To call one carcinoid and the other sarcoid prejudices too much, and to call the one spheroidal celled and the other spindle celled tells too little. Acute and chronic as descriptions would express the clinical course better than either.

Allied to the melanomas is a group of tumors which do not generally develop from demonstrable pre-existing lesions, but which show relationship to the melanomas inasmuch as many of them develop pigment at some stage. Those that do not develop pigment run a course parallel with those that do so that the identity of these types may be accepted. Since these tumor cells produce pigment the name "chromomas" is adopted, which is but a convenient abbreviation of the more correct term of "chromatophoromas." This designation is based on the assumption that the chromatophores are pigment-producing cells.

One quality of melanotic tumors has failed of general recognition. The connective tissue surrounding the nevus cells never attains the full development of acidophilic connective tissue. The degree of this abnormality is a measure of the likelihood of subsequent malignant development. That changes in the connective tissue are an essential process in tumor formation has been demonstrated. Whatever the factor in the failure in development that gives rise to the nevus cells also affects the development of adjacent connective tissue. The fact that the adjacent tissue does not attain full development itself is sufficient evidence that these areas are always points of potential tumor development.

Evidence that the tumors here called "chromomas" are really neurogenic is accumulating. Be this as it may, the term "chromoma" suggests the clinical relationship to the melanomas. Perhaps even the melanomas are neurogenic misplacements but fine speculations along this line belong to specialists in cytology.

The path of metastatic formation is often invoked in determining the nature of a tumor; the epithelial selects the lymph channels and the connective tissue tumors the blood vessels. The melanomas select at first the lymph vessels except in a small minority of cases. But curiously enough the violently malignant alveoli-forming tumors select the blood stream as the avenue of dissemination much oftener than does the slow-growing fibrotic type. This is but another sign of the independence of melanotic tumors of both carcinomas and sarcomas. Melanomas are melanomas.

Classification of the Melanomas. A useful classification must recognize the fact that certain benign pigmented tumors are more likely than others to become malignant and when they do become malignant, they follow diverging courses. Some remain always cellular, some begin as such and become fibrotic in the course of development. Some begin as spindle cells and remain so throughout the course of development of the tumors. Some chromomas begin as nodules attached to the skin while others originate deeper. These tend to become more fibrotic as the tumor develops. These variations are important in the early recognition of the nature of the tumor and must be kept in mind in attempting a classification useful in the clinic.

A. Benign Melanotic Lesions

1. Multiple
2. Solitary

B. Malignant Melanotic Lesions

1. Melanomas
 - a. Spheroidal celled (Melano-carcinomas)
 - b. Spindle celled (Melano-sarcoma)
2. Chromomas
 - a. Intradermic
 - b. Subdermic

BENIGN MELANOTIC TUMORS

One should always speak of benign melanotic tumors with some mental reserve. Here more than anywhere else in the whole field of oncology does vigilance produce a dividend. None are so innocent but that they may rise up sometime and smite their host. Fortunately the

various types show a varying degree of likelihood to developing into malignancy. Multiple pigmented lesions are less likely to undergo malignant degeneration than is a single lesion. If one is going to decorate himself with moles the more possible the better. This observation should not be overemphasized for one of many may become malignant but it is of



FIG. 107. Pigmented moles of the back. M., age 35. The smaller less pigmented lesions are flat, even with the surface of the surrounding skin. Some of the more deeply pigmented areas are elevated.

sufficient importance to warrant separate consideration of the multiple and solitary lesions.

Multiple Melanomas. Freckles cannot be considered a disease but they do present the simplest form of pigment concentration. Commonest in red-haired youths between the ages of 8 and 15, most pronounced in

the summer months they tend to disappear or lessen in intensity with the advent of winter and the approaching maturity of the individual. The increase of pigment is in the rete, not in any undeveloped cells.

The flat multiple melanomas are more permanent and may in their simplest form not be so far removed from freckles. They take on malignant changes less commonly than solitary moles and when they do so are apt to produce lesions which remain local for a long time. These multiple melanotic lesions seem to bear a close relationship to multiple neuromas. Not uncommonly the two conditions seem to be combined.

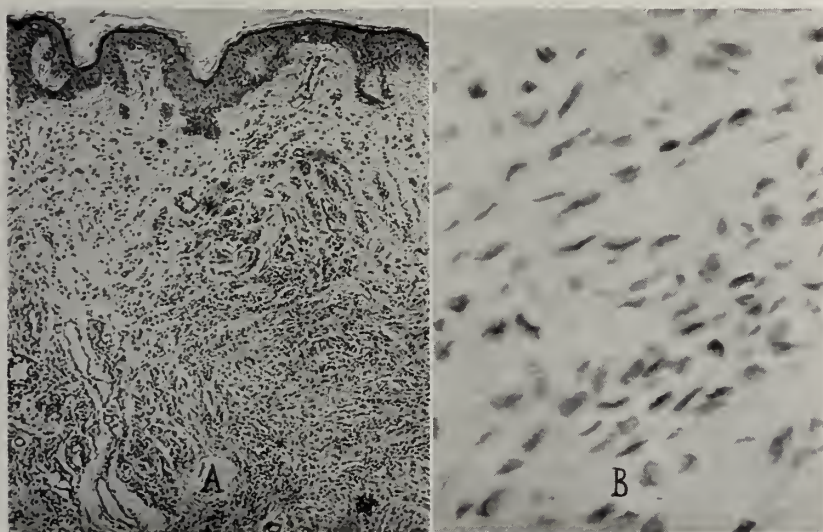


FIG. 108. Nonpigmented mole. Nevoid cells spindleform. *A*, low power; *B*, high power of connective tissue with spindleform cells. Intermingled with this are larger, more spheroid cells with granular nuclei. These suggest chromatophores.

Pathogenesis. The flat moles are commonest on the back and chest. They range from a few to countless numbers. They begin as flat areas varying in color from a light yellow to deep brown, even black. Commonly they remain so throughout life. In some instances they become elevated, producing rounded rough tumors (Fig. 107). They may cover wide areas and sprout hair. Sometimes they are linear and follow the general direction of a nerve trunk.

When certain members of these melanotic colonies increase in height and diameter they must be regarded as premalignant. On attaining malignancy the growth remains local for a considerable time and when inadequately removed recurs locally with persistency before actual

metastases occur. In this they differ from the malignancies which arise in the solitary melanotic warts.

Pathology. In quiescent stage the multiple benign melanomas present spots which may be slightly elevated but ordinarily they lie flush with the surrounding skin like colored tile in a floor. They may be firm to the touch but when not elevated present no palpable difference from the

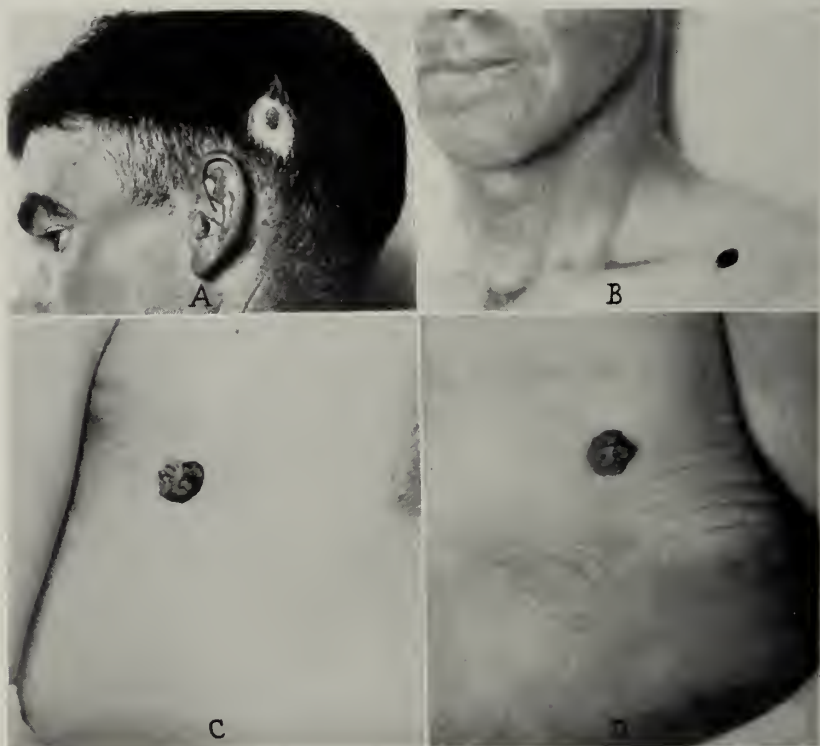


FIG. 109. Typical solitary pigmented moles located at regions where they are most likely to develop malignancy. *A*, on the temple; *B*, just below the clavicle; *C*, just in front of the axillary fold; *D*, just behind the external malleolus.

surrounding skin. As the point of malignancy is approached the lesion becomes firm and the surrounding skin reddened. When new nodules are formed in the region of the parent mole a malignant state has already been reached. Cross section discloses that the pigmentation is confined to the skin.

Histology. The epithelium covering these lesions may be hypertrophied and dips down into the skin but is seldom changed. Below the skin is a collection of pigmented nevoid cells. The cells in the multiple nevi

tend to spindleform (Fig. 108) intermingled with which are ovoid cells, resembling the chromatophores, especially when they are tending toward malignancy. Associated with these are the round cells of indeterminate type. Even microscopically it is not always possible to say if a malignant stage has been reached or not.

Solitary Melanomas. For reasons not understood solitary melanomas are much more prone to become malignant than the multiple. Equally obscure is the reason why tumors in certain regions are more likely to show a riotous development.

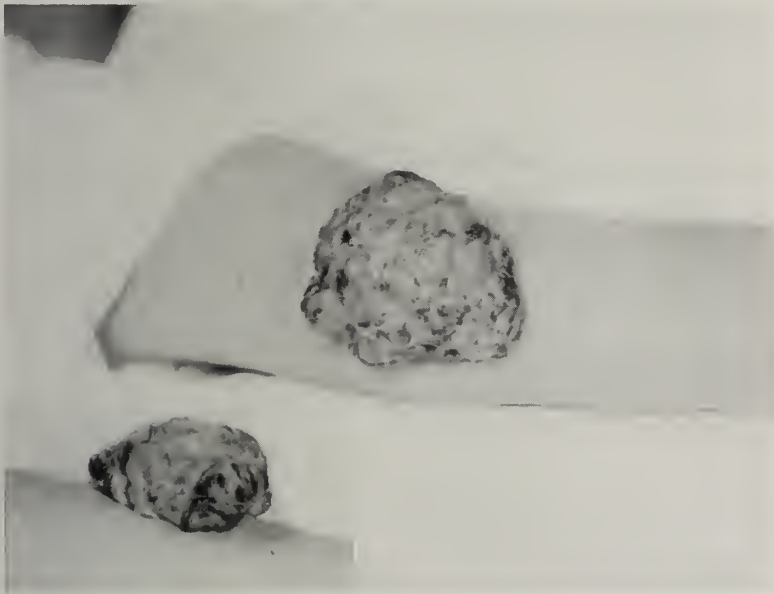


FIG. 110. Fungating melanoma. F., age 41. Large pigmented, pedunculated tumor which has been developing during the past ten years. Removed. No recurrence 7 years later. *Insert* shows another view of tumor.

Pathogenesis. The solitary melanoma should always be regarded as a precancerous lesion and be dealt with as such. It is usually elevated, rounded, even pedunculated, either of smooth outline or more or less bosselated (Fig. 109). They are most common on the temple, the shoulders, the clavicles, axillary fold, about the groin, and on the foot. Those situated near lymph gland groups are most apt to become malignant.

These tumors are usually observed first in early childhood but may become apparent only in later life. They may remain unchanged for many years, even throughout a lifetime but they are always a menace to their hosts.

Generally speaking they remain small but an increase in size does not always precede malignancy. This cannot be emphasized too strongly.

In rare instances the local tumor develops to considerable proportion, even to the size of a lemon, without evidence of clinical malignancy (Fig. 110). They usually ulcerate and an abundant inky fluid is discharged. This condition may exist for months, even years, before local or general metastasis begins. These tumors stand as connective links between the very malignant type which produce early metastases and the harder spindle celled melanomas which form metastases late.

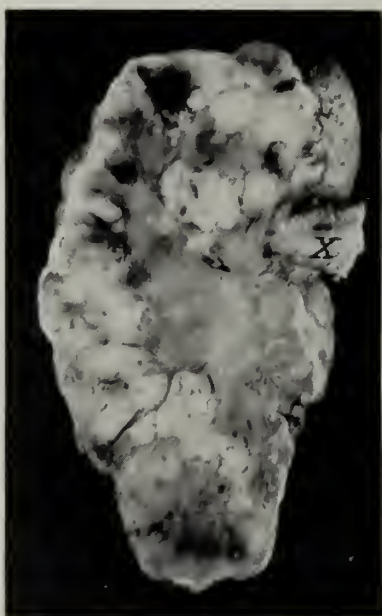


FIG. 111. Cross-section of a pedunculated melanotic tumor showing mottling. The small pedicle is shown at x. It is free from melanin and is composed wholly of connective tissue.

Pathology. The color varies from white to deep black. Some tumors show streaks and mottlings (Fig. 111). They are soft to the touch though some of them may be bedecked with a dense cornified epidermis. They are sharply circumscribed against the adjacent skin and are nearly always sessilated. Innocent tumors of this form and size can be diagnosed with certainty in cases where the patient remains free from recurrence after many years.

Histology. The finer structure of melanotic tumors differ with the age of the tumor and the age of the patient as well as with the varying

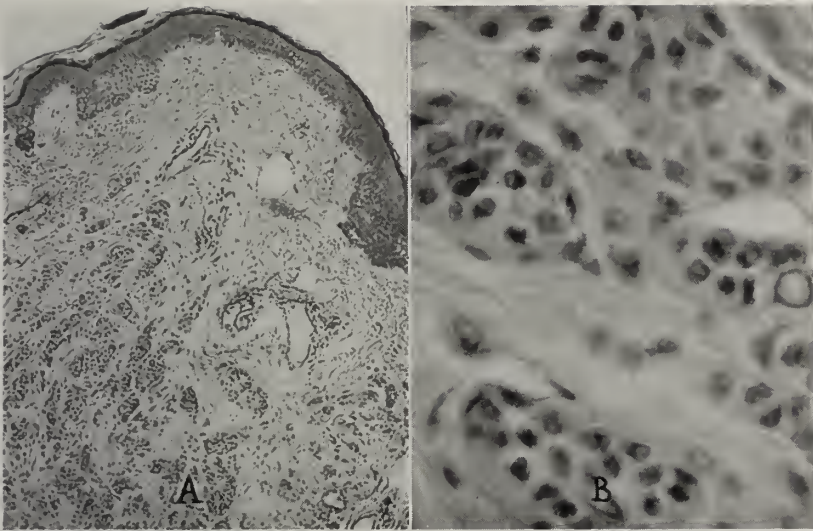


FIG. 112. Small pigmented mole from the back. *A*, low power showing the relation of the nevoid cells to the skin above. They are separated at all points from the epidermis by connective tissue, thus showing their genetic independence. *B*, high power: the nevoid cells are spherical without intermingling of connective tissue.

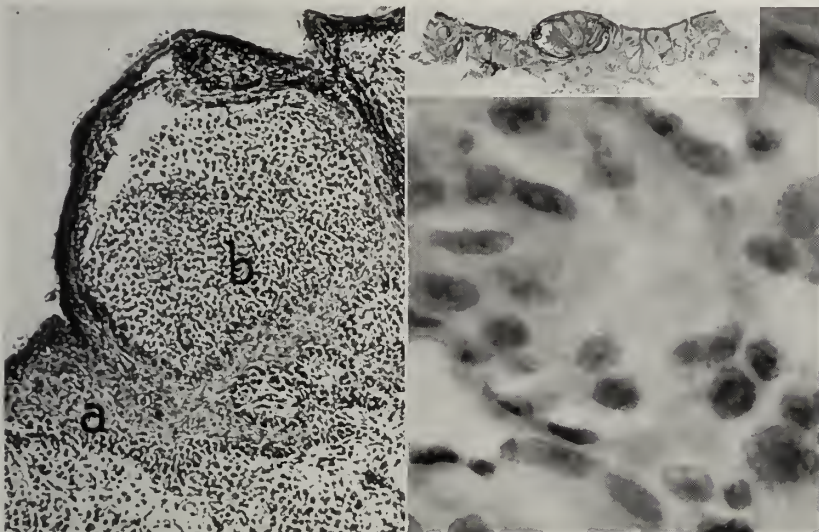


FIG. 113. Small pigmented wart undergoing malignancy. The primary tumor was the size of a grain of wheat: *a*, hypertrophied epithelium; *b*, deeply staining nevoid cells; at the right the same in higher magnification. Nothing positively indicative of malignant change yet there were metastases as large as walnuts. *Insert*, the cross-section of the tumor magnified 4 times.

cellular activity. Early the epidermis is but little changed and the pigmented tumor cells lie just beneath it and in the derma (Fig. 112). Finger-like cellular processes dip below and may appear connected with the sweat glands or the hair follicles. These columns, when cut cross-wise, appear as detached nests. In others no definite connection between pigmented and nonpigmented nevoid cells can be found, if they ever existed. The lymph and blood vessels seem to be uninvolved.

When the tumors increase in size it is due to increase of the nevus cells, pigmented or unpigmented. They become elevated, bosselated or more or less sessilated, and dip deeper into the surrounding tissue. The cell columns become elongated and invade the surrounding connective tissue. The pigment-containing cells are usually most abundant in the borders of the cell masses. Enlarged nevoid cells or the presence of pigment in the intercellular spaces suggest malignancy (Fig. 113). These changes may take place without obvious increase in size of the tumor in the vascularity of the surrounding skin.

In later life the connective tissue may increase and the cell masses become relatively reduced or the connective tissue may degenerate and the tumor become pedunculated. Local annoyance is increased and this often leads to meddlesome irritation. Such regressive changes are often misleading. Astonishing malignant possibilities are latent. I have seen a number of these assume malignancy when the pedicle was constricted with a string or cut off and the pedicle cauterized with carbolic acid, as once recommended by Crocker. Even the irritation of X-rays or radium may start these tumors on their destructive career.

MALIGNANT MELANOTIC TUMORS

I am convinced that the confusion in the discussion of melanotic tumors is due to the fact that writers have tried to force two different things into the same bag. Many able pathologists contend that all melanotic tumors belong to the epithelial group. All that one can admit is that they may spring from anlagen from which, if normal development had followed, would have developed into epithelial cells. One cannot admit that melanomas are derived from any cell which at any time even approached a normal cell. Let it be repeated, melanomas are the product of the nevoid cells which never have attained a degree of development which warrants their comparison with any normal structures. They are born outlaws and such they remain. There is more evidence that they are neurogenic than that they are epithelial. Those that contend that nevoid cells are terminal nerve cells which have gone away have initiated a hypothesis which cannot be disproved and there is

some circumstantial evidence to support the suggestion. True, some retain a spheroidal cell form and describe an alveolar arrangement, even to the metastases in the viscera, but this is not constant enough to warrant any conclusion as to their genesis. However this type and arrangement of cells gives them a clinical separation from those slower growing tumors with a spindleform cell, even in their metastases.



FIG. 114. Metastatic melanoma. M., age 23. He had had several operations for the removal of tumors behind the angle of the jaw during the past 2 or 3 years. Now there is a tumor in front of the ear. A small melanotic wart in the parietal region had not been discovered.

There is such a great variation in the clinical course of pigment-bearing cells that I have sought to find an anatomic basis for this difference. The rapidly growing type are made up of round cells with a tendency to alveolar formation while the more slowly growing form are spindleform in the degree that they are slowly growing. Therefore I have divided them into the round and spindleform types. This is desirable because of the great difference in the clinical course. The round celled form is always hopeless, the spindleform may in some instances be arrested by very wide local excision.

Spheroidal Celled Melanomas. These melanomas are derived from the nevoid cells of congenital pigmented papillomas, most often in isolated forms and most often from those located in certain anatomic regions. The spheroidal celled type are characterized by slight change in the parent tumor and early and extensive metastases.

Pathogenesis. The most common site of the primary tumor is on the scalp or temple, the neck and upper chest; not infrequently the inguinal region and more rarely on an extremity (Compare Fig. 109). These little solitary tumors may remain unchanged for years, may even regress and disappear entirely but they are a constant menace. With or without local



FIG. 115. Early changes in a pigmented mole. M., age 46. Had numerous flat pigmented warts over shoulder and upper back all his life. Recently one has become painful and has increased in size. Axillary metastases present.

change they may at any time be the source of malignant tumors. They should always be regarded as precancerous lesions.

Let it be repeated, metastatic tumors may be derived from these melanotic tumors without any gross change in the primary lesion (Fig. 113). So common are melanomas that whenever enlarged lymphglands or multiple tumors are encountered, search should always be made for a solitary melanoma, or for a scar remaining at a site from which one has been removed (Fig. 114). The local tumor may show irritation about its base and an indurated and reddened skin (Fig. 115). These slight local changes are of the greatest significance: almost certain evidence of malignancy. The formation of new nodules in the neighborhood of the

tumor is unusual in this type of melanoma unless they have been irritated or imperfectly removed. In such cases extensive new tumor formation may take place near the site of the original tumor.

The failure to remember that little or no local change may presage the advent of malignancy may lead to embarrassment. I once removed a supraclavicular tumor believing it to be benign. A small melanoma just back of the shoulder was overlooked until the nature of the supraclavicular tumor was determined. Another time I diagnosed a bleeding tumor of the kidney a hypernephroma, overlooking a melanoma of the shoulder which had been removed by tying a string about its pedicle.



FIG. 116. Melanoma of the upper arm with metastases in the axilla. M., age 56. Complains of a tumor mass which has appeared in the axilla during the past four months. That he had had a pigmented wart removed from his upper arm was a forgotten event. Radical operation. Prompt recurrence.

When a pocket of enlarged lymph glands is encountered usually casual inspection reveals the source of the trouble. Other possibilities however must not be forgotten. I once saw unilateral Hodgkin's disease localized in the cervical region in a man who had a pigmented nevus in the temple wrongfully suspected of having caused metastases.

The frequency with which the melanomas are started on their malignant course by ill-advised attempts at their removal such as caustics, tying a string about their bases, or some electrical process including radiation which irritates but does not destroy, is not sufficiently appre-

ciated. These meddlesome procedures cause more deaths in my experience than cancer of the uterus.

Metastatic tumors may be so large and contain so much pigment that their black color may show through the unopened skin. On the other hand the metastatic nodes may be entirely pigment-free, so that even with tumor in hand one may be in doubt as to its source.

The occurrence of visceral metastasis must not be forgotten. These secondary nodules are usually small but so numerous that they may cause a general enlargement of the organ. Hemorrhage from mucous surfaces,

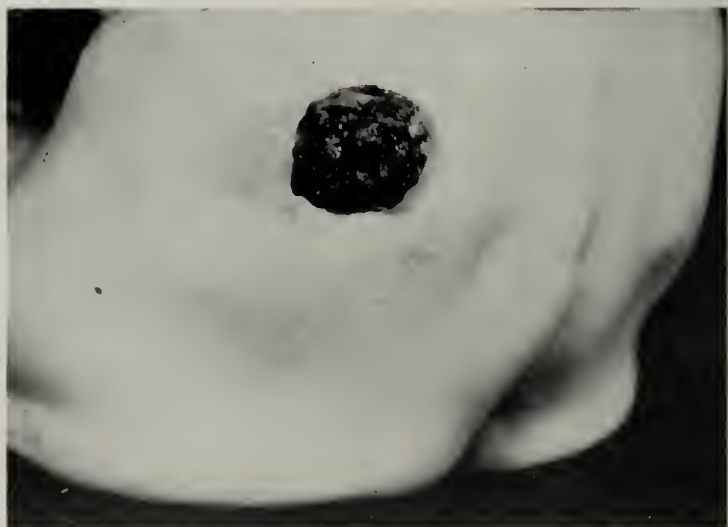


FIG. 117. Large bleeding melanoma of the back. F., age 80. During the past two years a small black tumor on her left hip has grown to the size of an egg. The surface has been bleeding some during the past few months. Freely movable with the skin. Wide excision. Metastases in inguinal lymph glands in six months.

kidney, bowel, bladder, may be the first evidence of the disease. Metastasis in bones, particularly in the spine, is not uncommon. Obscure brain disease likewise may be the first intimation that the individual is sick. In fact so ubiquitous are the localizations of metastases that in any obscure disease it is worth while to give thought to the possibility of a melanoma. Wart hunting may be a very profitable diversion when one is confronted by obscure disease.

The course of the round celled melanomas is rapid. Injury or irritation of the primary tumor may show gland metastasis in three or four weeks and death may follow in as many months. This is particularly true when the blood stream is the avenue of dissemination. In such cases

countless tumors form in the skin and viscera with no involvement of the lymphatics. I once had a patient with a melanoma of the temple which was removed by a cancer paste. Within 3 months more than a thousand metastatic nodules were counted in the skin. All the viscera, even the heart, were studded with little tumors.

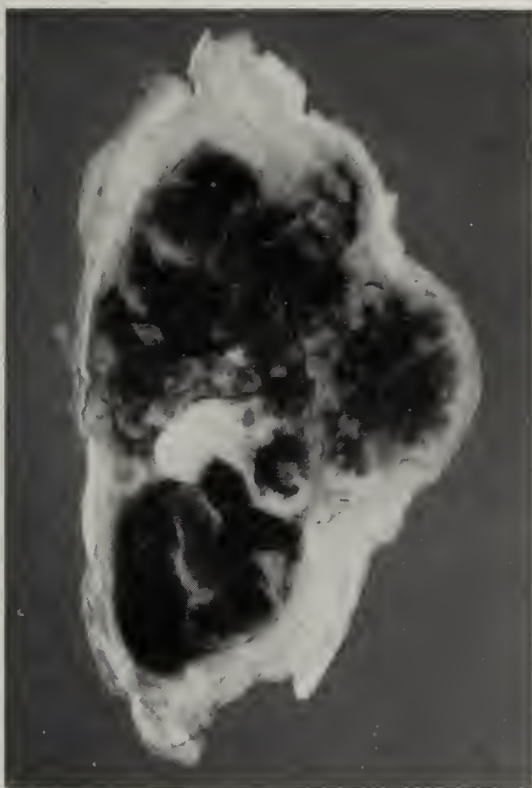


FIG. 118. Metastatic melanoma of the groin. The deep black color was evident through the intact skin.

Often there is a negative history as to the previous existence of a wart. Therefore the surgeon must not fail to search the drainage area for small scars. If one is discovered the patient may then recall that an insignificant wart was removed by cauterization, by tying a string about its base, or whatnot (Fig. 116). I have repeatedly cleared up perplexing situations by such quests. A spinal lesion regarded as tubercular was explained by finding a small scar. Autopsy revealed a melanotic lesion in a vertebra. I suspect that some of the unexplained visceral melanomas have such

antecedents. An internationally known internist reported a primary melanoma of the liver, ignoring wholly the history of an eye removed three years before for a melanotic tumor.

Pathology. The beginning, as noted above, of malignancy is manifested by induration about the base or the development of new tumors. There may be an increase in its blackness, a shiny appearance like a perspiring darky's nose (Fig. 117). A quiescent melanoma does not have this shiny appearance. The new tumors about the primary growth are certain evidence of malignancy. They may or may not be pigmented. When deeply seated they are more obvious to palpation than to inspection.

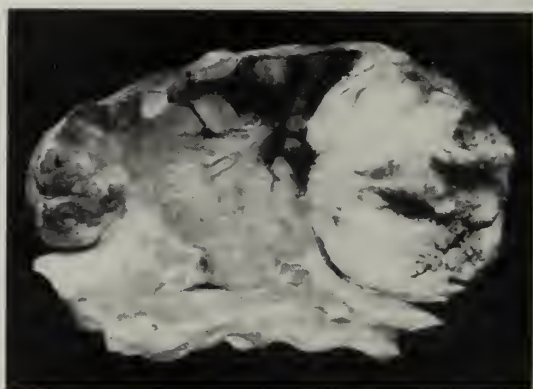


FIG. 119. Cross-section of a large melanoma. The various degrees of pigmentation are shown. The right lobe shows hemorrhagic infarction.

The metastatic glands are firm elastic. They may form a chain, as in the neck, or a conglomerate mass as in the axilla, or in the groin. The entire chain of glands may be of the same size suggesting simultaneous invasion. The pigmentation may be more or less intense than the original tumor. Indeed it may be so intense that it fairly shimmers through the skin (Fig. 118). This may be the first clue to the nature of the tumor.

On cross-section the primary tumor may show but little change but usually it extends more deeply into the subcutaneous tissue than a non-malignant melanoma. When large they are usually mottled (Fig. 119), but may be an intense black throughout or may contain no pigment. Localized extension of the growth may be a continuation of the primary tumor or a separate tumor or a constellation of tumors. The multiple recurrence in this form of tumor is rare. In the type soon to be described

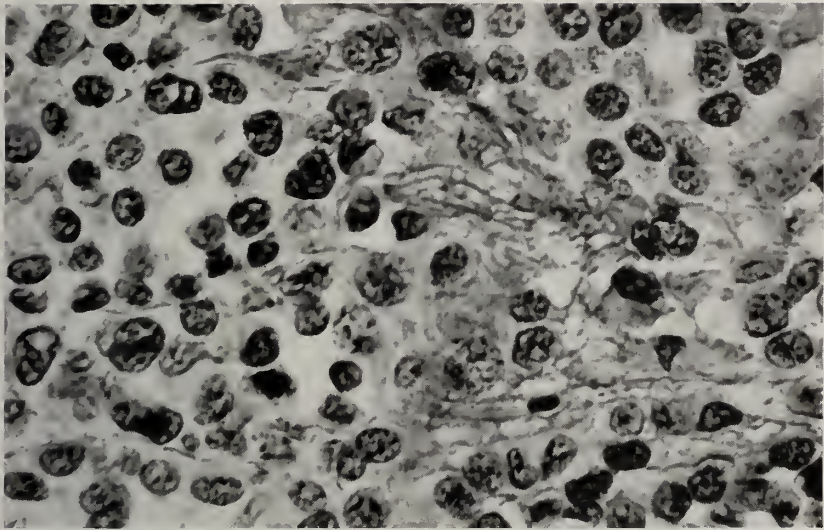


FIG. 120. Typical structure of the most malignant type of melanoma—the large round cells with little connective tissue. The cells of melanomas have a characteristic appearance more easily perceived than described. The cells are spheroidal, have granular nuclei and clear protoplasm. They are usually arranged in pseudo-alveoli by sparse connective fibres which may pass between individual cells.

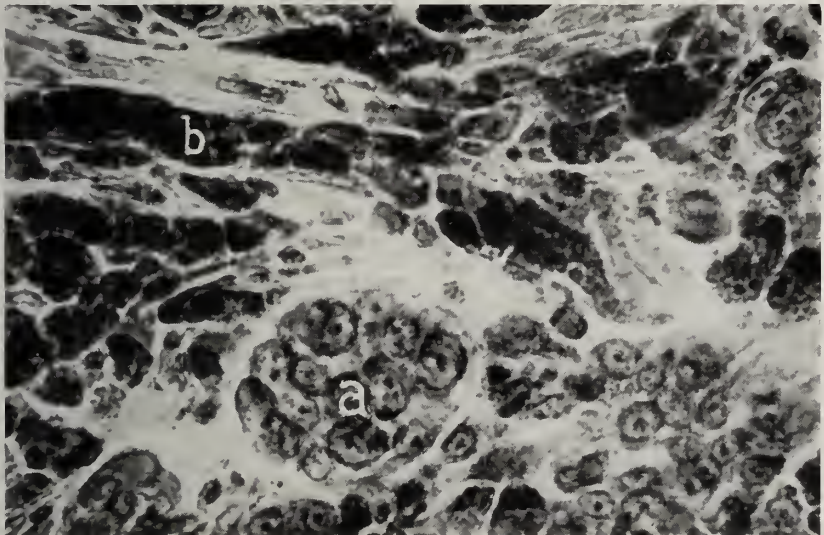


FIG. 121. Beginning malignant melanoma; *a*, the tumor cells are spheroidal for the most part; *b*, extensive intercellular deposit of pigment. The arrangement of the cells is characteristic of these tumors without the presence of pigment. The pigment may be contained in the protoplasm of the cells or in the spindleform cells between them.

it is the usual occurrence. The metastatic tumors are usually softer than the original tumor and less black. But an amelanotic or yellowish primary tumor may produce metastases with much pigment.

Those cases, in which countless metastatic tumors occur in the skin, usually show but little pigment. Nature does not seem to produce pigment fast enough to color all the tumors. This must be remembered lest their relation to a pigmented tumor be overlooked. The cells are carried through the blood-stream and lodge in the small vessels of the skin. Visceral metastases are relatively small in size but countless in number

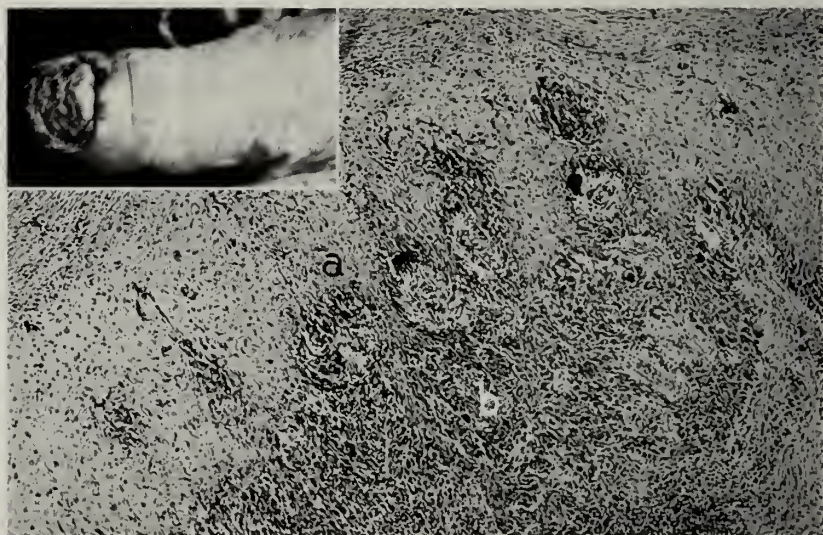


FIG. 122. Melanotic whitlow. F., age 46. For a number of months there has been a painful inflammation under the thumb nail. *a*. Epidermis; *b*, pigmented cells directly springing from the epidermal cells. *Insert*, gross appearance.

and involve the organs more or less uniformly. Visceral metastases are not always small. The liver may present larger masses easily palpable through the abdominal wall. I once saw a melanoma of the liver as large as an orange secondary to a small tumor of an eye. Melanotic metastases in the liver lack the dimpling common in metastases from obscure carcinomas of the digestive tract and are usually more uniform in size than the primary tumors of the liver. Of course if any of the nodules are pigmented the recognition is easy but often they are without pigment. When they lack definite pigmentation the color is usually more of a yellowish tinge than metastases from visceral disease. Metastases in the kidney are less common and the numerous solitary nodules promptly awaken the surgeon once the kidney is exposed.

Unfortunately such errors as these do not make complimentary records for the surgeon and consequently are not commonly reported. The pathologist must keep an eye on the need of pleasant relation with the various members of the hospital staff, hence he also may be silent.

Histology. The typical cell of round celled melanomas is large and spheroidal with a large granular nucleus (Fig. 120) and sparse intercellular connective tissue. Generally speaking an increase in pigmentation may be the first sign of impending malignancy (Fig. 121). The isolated cell

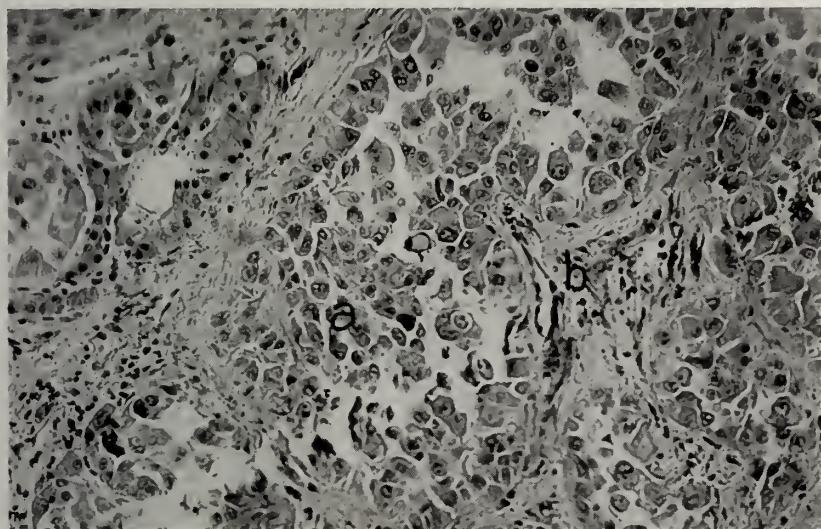


FIG. 123. Liver metastasis from a melanoma of the temple: *a*, cell nests without interstitial connective tissue; *b*, fibrous septa dividing the cell masses into nests.

columns or cell nests show an increase in volume, the nuclei stain more deeply. The activity is confined to the nevus cells. When the epidermal cells become active they do so in response to hyperactivity of the neval cells below just as they do over any chronic irritative process.

In very rare instances let it be recorded the epithelial cells seem to be the active instigators, as Unna contended, of the tumor process. In such cases the newly formed cells are seen to be direct outgrowth of the epidermal cells (Fig. 122).

It is characteristic of the round celled type of melanotic tumors that the cells form columns or nests surrounded by connective tissue but not separated by it. This alveolar formation is particularly impressive in metastatic nodules in the viscera (Fig. 123).

As the tumor extends the lymph vessels are involved as is evidenced by their close association histologically and by the extension of the tumors along the lymph vessels. The local invasion of the blood vessels cannot often be made out but the dissemination by way of the blood stream soon becomes obvious. In the metastatic nodules quite commonly the vessel walls seem made up of large tumor cells without the participation of either connective tissue or endothelium.



FIG. 124. Spindle celled melanoma of back. M., age 60. A year ago had an injury to his back. A black mole was torn off by the injury. A month later a lump formed at the place where the mole had been. Later on other lumps appeared. Now two large lumps are present which can be seen and numerous smaller ones which can be felt.

Spindle Celled Melanomas. This variety of melanotic tumor is characterized anatomically by its tendency to form spindle celled, even fibrotic tumors, and clinically by extensive local invasion and relatively late metastasis. Their early recognition is imperative because very wide local excision is sometimes curative.

Pathogenesis. These tumors begin in pre-existing lesions containing nevus cells. The initial lesions are usually little elevated, and but slightly pigmented. They form globular tumors, the size of a hickory nut or larger, which protrude from the surface of the skin (Fig. 124). Early secondary tumors near the parent tumor are common. They are most

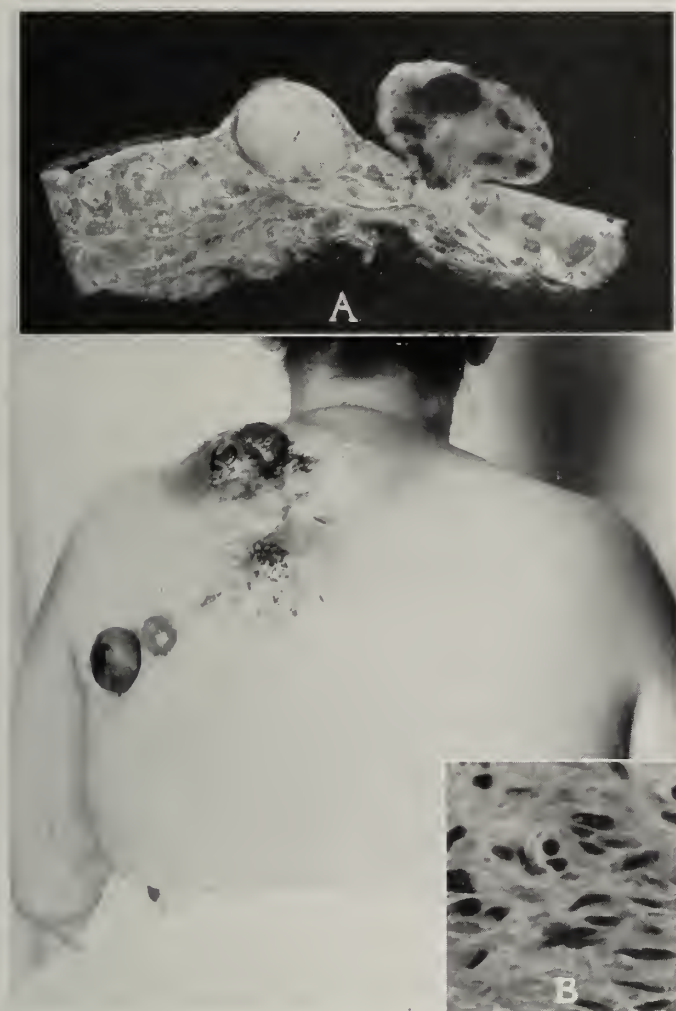


FIG. 125. Recurrent melanoma of the shoulder. F., age 46. Ten years ago had a little red tumor removed. It remained healed three years. Wide excision with subsequent skin grafting was followed a year later by local recurrence and metastasis in the axillary lymph glands. *Insert A* shows a small white tumor within the skin and a pedunculated pigmented one. *Insert B* shows the typical spindleform maintained throughout the various lesions.

frequent about the shoulders (Fig. 125) and extremities (Fig. 126) but may occur on any part of the body. They do not ulcerate early but may ultimately do so. When destroyed by therapeutic means they are prone to recur locally with persistence forming daughter tumors in direct apposition to the mother tumor or at some distance from it, hence the necessity

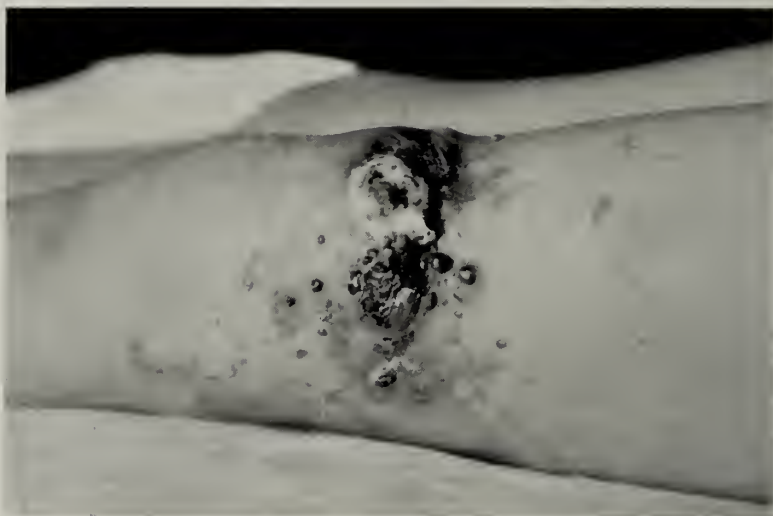


FIG. 126. Recurrent melanoma of the thigh. M., age 60. He noticed for three years a small elevated lesion above the knee-cap on his right thigh. It was excised with a small margin of skin. It recurred a year later producing local ulceration and a multitude of small globular tumors in the neighborhood.

of wide local excision. Sooner or later metastases form, first in the neighboring lymph glands but later in the viscera, but visceral metastasis is much less common and occurs much later than in the round celled form. A number of years are required for the disease to run its course. Generalized metastasis, by no means uncommon in the round celled form, does not occur in this type.

Pathology. These tumors produce elevated nodules often covered with skin which is but little changed early in the course (Fig. 124) but

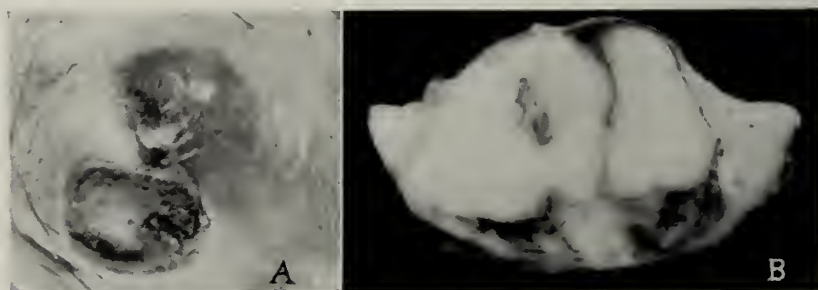


FIG. 127. Top view and cross-section of an ulcerating melanoma. *A*. Surface view of tumor which has destroyed the skin; above the skin is attenuated but is not destroyed. *B*. Surface skin is much thinned, the tumor mass colorless and lobulated. Below the tumor is hemorrhagic and contains melanin.

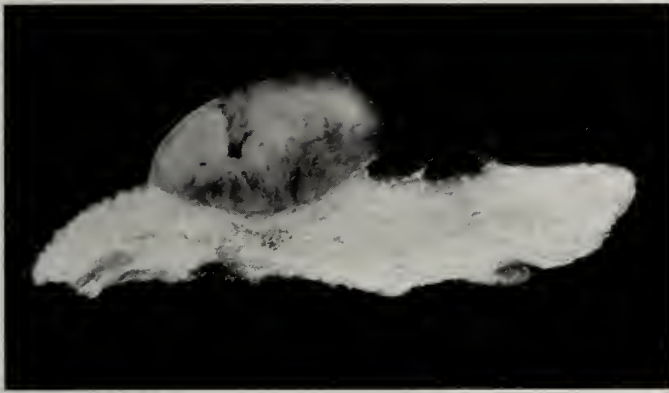


FIG. 128. Cross-section of melanoma. The larger is the primary and is mottled. The secondary is small and intensely black. The dermal origin of both is well shown.

may become attenuated, reddened, and even ulcerated later (*A*, Fig. 127). These tumors may be obviously pigmented (Fig. 128), but commonly it is not so and they appear only as globular white tumors (*B*, Fig. 127). Often the pigmentation may be obvious in the secondary tumors when the primary show but little pigment (Fig. 128).

The cross-section shows more or less globular tumors which may be lobulated (Fig. 127). Pigmented areas may be seen on cross-section which

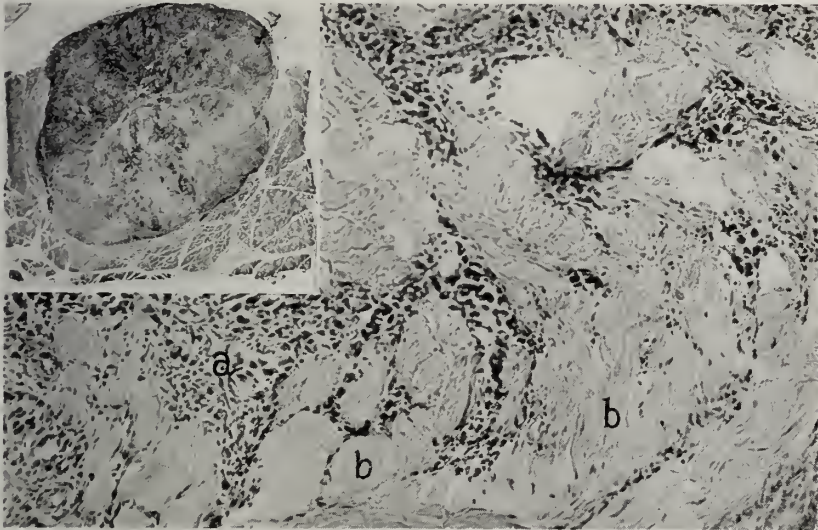


FIG. 129. Invasion of surrounding tissue by tumor cells. *a*, tumor cells; *b*, wide invasion of the surrounding subcutaneous connective tissue. *Insert*, gross appearance of tumor enlarged 10 diameters.

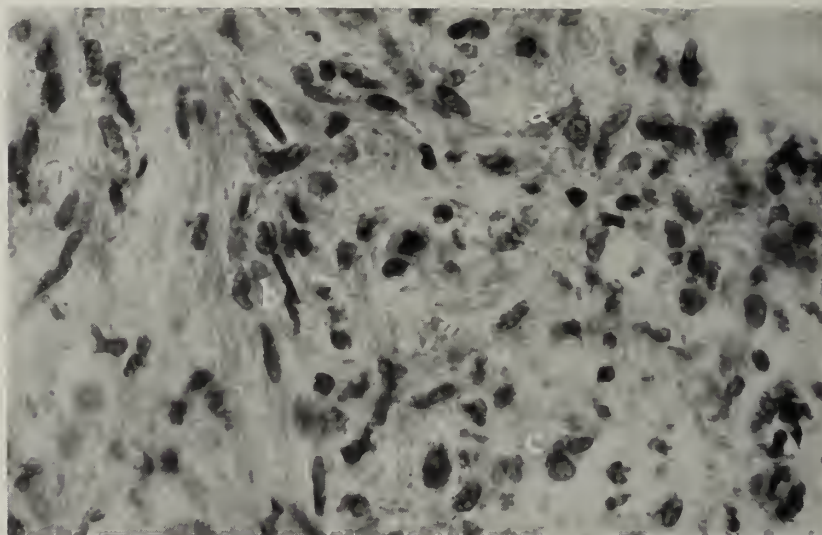


FIG. 130. Spindle celled melanoma. The cells for the most part are spindleform with much intercellular fibrous tissue. The spheroid cells are unusually numerous in this slide: *a*, spindle cells; *b*, connective tissue; *c*, spheroidal cells. Longitudinal section of spindle cells may be mistaken for round cells.

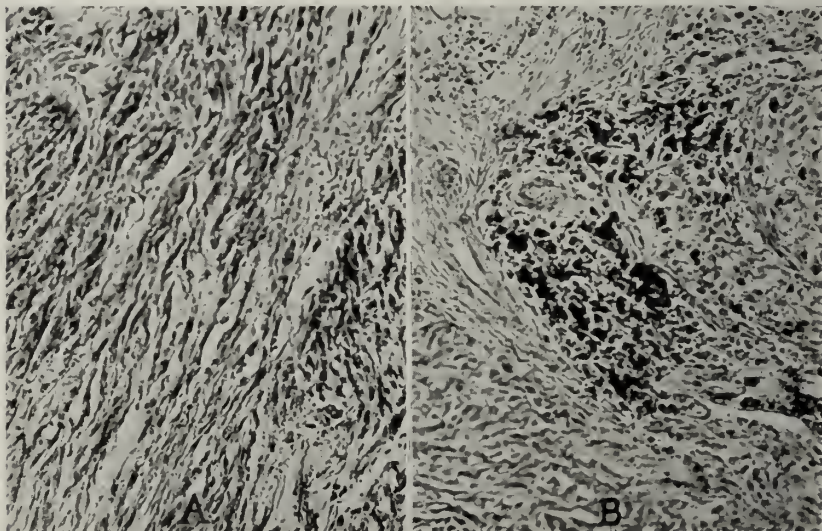


FIG. 131. Fibrocellular type of melanoma. Very slowly growing melanotic tumor of the shoulder. *A*. The most of the tumor is made up of long spindleform cells with narrow long nuclei. *B*, fibrilform for the most part, dense pigmented area in the center. This tumor had few such areas.

were not visible when the tumor was in situ (Lower part, *B*, Fig. 127). Frequently the tumor is mottled. On the whole the presence of pigment is less impressive than in the group previously described.

The primary tumors sometimes give the impression of complete encapsulation (*Insert*, Fig. 129). Slides from such tumors invariably show wide invasion of the adjacent tissue by the tumor cells (Fig. 129).

Histology. The dominant cell is spindleform. This is impressive from the beginning (Fig. 130). Though globular cells are sometimes present par-

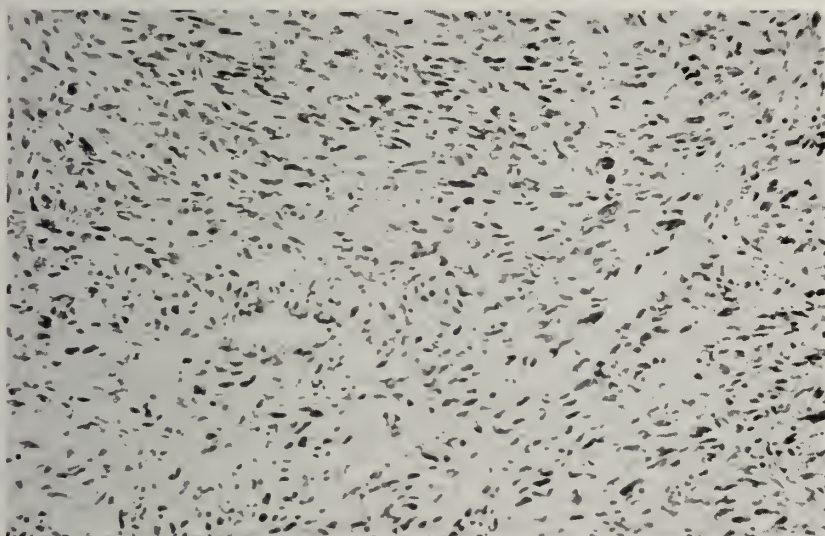


FIG. 132. Liver metastasis from melanoma of the skin. The numerous melanotic nodules in the liver were made up of spindle cells varying some in size and stainability. The vessels were numerous and thin walled.

ticularly in early lesions the dominant cell tends to become more spindleform later. Sometimes the cells are stellate. The tumor may be distinctly fibrillar particularly in the slowly growing forms (*A*, Fig. 131). The pigment usually lies in the interstitial spaces (*B*, Fig. 131). They rarely show alveolar formation, common in the round celled type. The spindle form of cell is retained in the visceral metastases (Fig. 132).

Chromomas. The tumors which I have placed under this heading stand midway between the spindle celled melanomas just considered and the neuromas.

In contrast with the spindleform melanomas the chromomas are slowly growing tumors which tend to local recurrence with relatively early metastases by way of the lymphatics. For this reason it seems

justified, for clinical reasons alone, to describe them in a separate group. Quite in contrast with the melanomas they are not developed from a previous lesion but arise in areas of skin previously normal. They grow up from beneath and destroy the skin before their advancing border. Their relation to the melanomas is attested by the fact that they produce



FIG. 133. Chromomas of the forearm and arm. *A.* F., age 36. Trouble began 2 years ago; noticed a small knot on the forearm. The surface became red and a doctor cut the tissue out. It remained healed five months. Now there is a nodule the size of a split hickory nut over which is an ulcer the size of a finger nail. The tumor is unattached to the skin and is firm, painless and does not bleed. *B.* M., age 32. Two months before he consulted his physician he noticed a tumor one-half the size of an egg three inches above the elbow. The tumor was excised. Healing was slow and a tumor three times the original mass filled the excavation. Two months later the tumor was again removed. It was separated with difficulty from tendons and nerves. The photograph was taken four months after the second operation. An irregular bosselated mass protrudes from the wound. The nodulations are dense, elastic, do not bleed on manipulation and are quite sensitive to touch. The skin border is thickened, but macroscopically and on section is shown to be quite free from the growth beneath.

pigment at some time in their growth in many instances. Certain large ovoid cells found quite regularly in the early stages suggest a relationship with the chromatophores which seems to warrant the designation applied to them. These cells are quite like the clasmotocytes of Ranvier with which I had much to do during my investigations on the peritoneum. Recently published investigations make me suspect that both the

melanomas and these chromomas will ultimately be brought into the neurogenic fold.

The chromomas may be divided into two groups. The one group, the *dermal*, begins as isolated tumors which seem as if set into the skin. This type is found sometimes on the trunk, oftener about the shoulders and on the extremities. The other and much the larger group, the *subdermal*, first appear as isolated subdermal tumors in previously unaffected areas. These destroy the epidermis secondarily. These tumors are found chiefly on the lower extremities, seldom on the trunk, never on

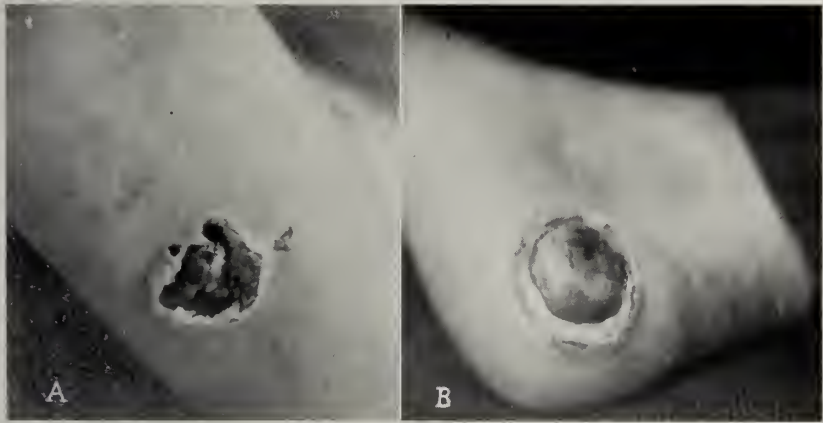


FIG. 134. Chromomas of the foot. *A.* M., age 50. Three years ago patient noticed a black spot on sole of foot in front of heel. It has grown gradually. No pain. Is now ulcer size of a dime. The border is irregular and undermines the skin. The base of ulcer is made up of coarse granulations of a deep red, glistening color. These granulations are elastic rather than dense, do not bleed easily on touch and are not sensitive. *B.* M., age 64. For several years he has had a gradually enlarging ulcer below the external malleolus on the left ankle. There was a hemispherical mass 3 cm. in diameter projecting from a defect in the skin, bordered by a zone 1 cm. wide, from which the epidermis had exfoliated. The tumor was deep red, granular, elastic, clean, and did not bleed on touch. Five years later nodules appeared in the abdomen and attained the size of cocoanuts before death.

the head and neck unless certain pharyngeal tumors shall prove to belong to this group. The chromomas further declare their allegiance to the connective tissue tumors by their close relation to the fibrosarcomas of the skin, the bald-headed sarcomas, presently to be described.

Pathogenesis. Because of the differences in their life history the genesis of these two groups must be described separately.

The Dermal Type. Those developing in the skin without pre-existing skin lesions produce early protruding tumors (Fig. 133). The primary lesion may differ but little from the spindle celled form of melanotic

tumors derived from nevoid cells. However, they tend to be flatter, may not at all be elevated above the surrounding skin and they are free from pigment. Very early the tumor is more impressive to the touch than to the sight, giving the impression of a hard object set into the normal skin.

The primary nodule increases in size without destroying the covering epidermis. These may attain the size of a hickory nut, even a walnut, without other change. The covering skin ulcerates sometimes in the early stages (Fig. 133). Other nodules may form in the neighborhood



FIG. 135. Chromoma of the foot with lymph gland metastases. M., age 56. He comes because of a gradually growing mass in the right groin. It is made up of a pocket of nodules the size of a walnut. Neither the patient nor his surgeon had discovered the primary tumor on the sole of the foot. *Insert*, the primary tumor life size.

(*A*, Fig. 133). Sooner or later metastases form in the neighboring lymph glands. When the primary tumor is agitated or inadequately removed, the development of accessory tumors may take place (*A*, Fig. 133), but usually there is but local recurrence. Often the disease remains localized for many years, even following successive removals, before metastases occur.

The Subdermal Type. These tumors begin as subcutaneous tumors and destroy the skin secondarily (Fig. 134). After a time they destroy the covering skin and the tumor sees the light of day. It may appear first as an ulcer. The tumor itself lies within a punched-out area of skin

giving the appearance of a granuloma (Fig. 134). Later on it may form a more or less protuberant mass.

The tumors usually require months, even years, in their development. Sooner or later metastases occur, at times in the line of lymphatics where there are no lymph glands but oftener the adjacent lymph glands are first affected. The primary tumor in rare cases may be so small as to have escaped observation and the first evidence of disease may be a massive metastatic tumor (Fig. 135). The ultimate course is progressive despite the slow growth. These tumors are relentless. Even amputation for apparently small tumors is powerless to stay the disease, though it may prolong its course—in one of my cases for nearly twenty years.

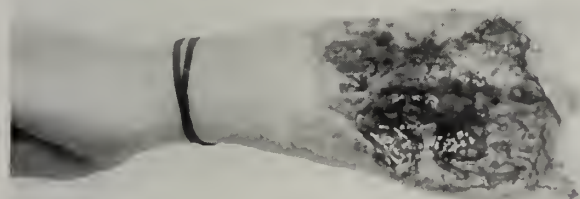


FIG. 136. Chromoma of forearm. M., age 30. Railway mail clerk. Two years ago he noticed a painless, round, firm tumor on the inner surface of his forearm. He had received a contusion in a railway accident some time previously. This tumor was removed but the wound did not heal and later a new tumor protruded from the wound. The ulcer was the size of the palm of his hand and occupied the radial side of the forearm. The outline was irregularly spheroid. The borders were somewhat overhanging and infiltrated. The body of the ulcer was lined by coarse granular elevations of a deep red color. They did not bleed on touch, but bled when the dressing was removed. The process from start to finish was entirely painless. When last examined the ulna and radius were exposed for a distance of four inches. He still followed his occupation on the mail trains.

Metastases in both occur sooner or later. They are hard, generally discrete and more or less movable.

The lymph glands may become extensively involved. In one of my cases, in which I did an amputation for an ulcer of the foot the size of a quarter, metastases developed in the groin, then in the retroperitoneal lymph glands, until at the end of five years his abdomen felt like a sack full of somewhat diminutive cocoanuts. In but one of my cases was the first metastasis in the mediastinal glands.

Nodules may develop along the course of the lymph channels before the lymph glands themselves are involved. This may be the first clue to the nature of what appears to be a painless plantar wart. For instance, in chromomas of the foot nodules may be felt along the course of the

lymphatics in the calf and thigh before the inguinal lymph glands become palpable. These metastases are confusing if the primary tumors are overlooked or improperly evaluated, because of their small size or because of temporary cure by operation. This development of metastases in the lymph channels explains why even amputation is so futile.

The huge retroperitoneal metastases may cause embarrassment of the fecal current and in one of my cases complete obstruction. Metastases within the mediastinum may obstruct the circulation or even the respiration. Those occurring in the liver seem to cause no disturbance, being generally incidental autopsy findings.

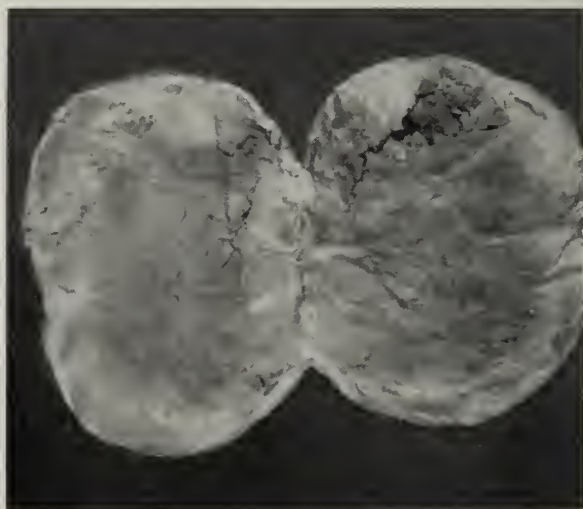


FIG. 137. Cross-section of an inguinal lymph gland of the groin in chromoma of the foot. The dense parallel fibre bundles are well shown.

On the arm the chromomas run a less typical course. They may first present themselves as a small subcutaneous nodule, then as ulcers (Fig. 133). They resemble tuberculous ulcers except that their borders are hard from the first and the surrounding skin remains white, unresponsive. They develop slowly, painlessly, but relentlessly. One of my patients continued his occupation of a railway mail clerk after both ulna and radius were exposed by the progressive ulceration (Fig. 136). Years may pass before ulcers of a considerable size are produced.

Pathology. Those tumors which begin in the skin produce globular, firm masses firmly attached to the skin. It is only when extensive invasion has occurred that they become attached to the deeper structures.

On section these tumors show a more or less spheroidal outline, but

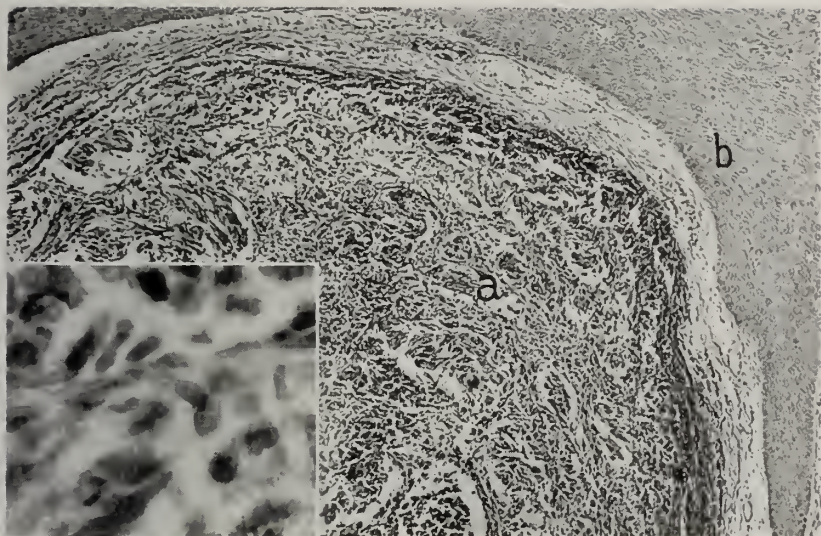


FIG. 138. Chromoma of the foot: *a*, the tumor mass is made up of whorls of spindle cells free from pigment; *b*, the epidermis being destroyed by the advancing tumor cells, *a*, but are not invaded by them. There are connective tissue fibres between them. *Insert*, high power of same showing spindle cells with large ovoid nuclei.

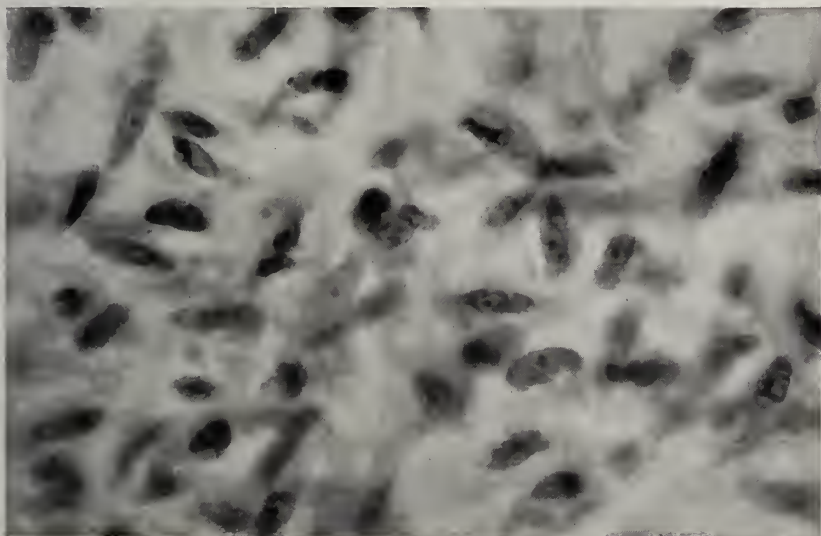


FIG. 139. Chromoma of the calf. Spindle cells with ovoid granular nuclei with deeply staining nucleoli. Smaller cells with uniformly staining nuclei lie between. The patient lived nearly 20 years after the first operation. Gradually enlarging tumors in the abdomen were noted several years before death.

without true encapsulation. Usually there is no line of demarcation between tumor and surrounding tissue.

When the tumor destroys the skin by protruding upward the firm mass is characteristic. It is not sensitive to pressure and does not tend to bleed. It is firm but not so hard as cancer and looks like granulation tissue.

On cross-section the development of the tumor independently of the skin is apparent. They sort of push through the skin like the tip of the finger through a wet blotter. The tumors are firm and grate under the

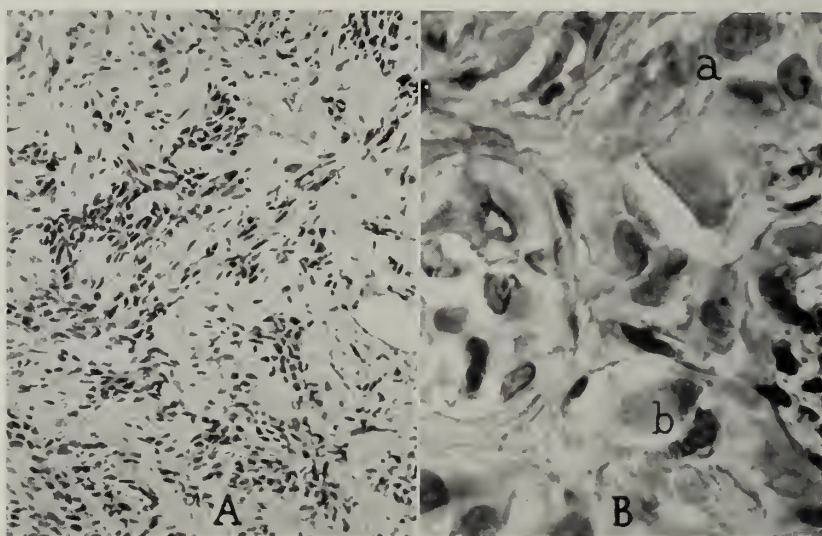


FIG. 140. Chromoma of the forearm (see Fig. 133). *A*. Ovoid cells appear in clusters between heavy bundles of connective tissue; *B*, the same, high power; *a*, well preserved chromoma cells; *b*, several cells undergoing degeneration.

knife when cut. In harmony with this the glistening fibrous bundles of connective tissue are visible. The metastases present a like picture.

The metastases are hard, fibrous and commonly contain no pigment. The arrangement of the cells in parallel bundles is particularly obvious (Fig. 137).

The microscopic picture of chromomas is usually that of a fibrosarcoma with or without pigment. The tumor appears to be pushing itself through the overlying epidermis (Fig. 138).

The typical chromoma cell, as I perceive it, is a fairly long spindleform cell, apparent in teased preparations, with large granular nuclei with deeply staining nucleoli (Fig. 139). In beginning tumors these cells are in evidence. Later in the course of development after the tumor becomes

fibrous and particularly in metastases these cells may not be in evidence. Usually imbedded in fibrous tissue, areas remain which show the cells (Fig. 140). In rare cases there is an alveolar arrangement of the cells in the primary tumor, less often in the metastasis but occasionally in both.

It is worthy of note that when v. Recklinghausen's disease becomes malignant the histology is similar to this form of pigmented tumor. This



FIG. 141. Bald-headed sarcoma of the abdominal wall. M., age 54. Gradually developing tumor for 10 years. The tumor is hard, the covering skin is thinned and reddish in color. *Insert*, dense fibrous tissue with spindleform nuclei except in certain clusters where they are ovoid.

may be regarded as further evidence that they are closely associated with the nerves.

FIBROSARCOMAS OF THE SKIN

(Bald-headed Sarcomas.) Since these tumors bear a resemblance to certain forms of melanomas, an account of them may be appended here. These tumors are not rare but they have received but little attention from writers and they seem to be generally misjudged by surgeons. I have

seen 28 of them in the past 30 years. They occur chiefly on the trunk. They are most common about the inguinal region, less common about the clavicle and about the buttocks. I have seen two on the thighs and one in the region of the mastoid process.

Pathogenesis. The characteristic factor of these tumors is their attachment to the skin. Because of the close association to the skin both the dermis and particularly the epidermis is much attenuated (Fig. 141). The tumors are elevated above the surface of the surrounding skin. The



FIG. 142. Recurrent bald-headed sarcoma of the flank. F., age 42. Tumor was shelled out one year previously. Rapid return of a nodular growth. One of the nodules had perforated the skin and was oozing constantly. No recurrence after 12 years. *Insert*, the slide shows a typical spindle celled sarcoma.

combination of these two circumstances make them as prominent as the bald pate of a male attendant at a woman's convention. Because of this the term "bald-headed sarcoma" is used in this clinic; an expressive, although a rather inelegant, designation.

They begin as small tumors, usually noted when no larger than a walnut. The growth is usually slow. After 5 to 20 years they attain the size of an apple or orange. Though intimately attached to the skin they glide freely over the underlying fascia.

After many years they are prone to become more cellular and then interstitial hemorrhages and subsequent ulceration of the skin may

follow. Once ulcerated they continue to exude a blood serum until removed.

They appear to be encapsulated but when shelled out, even if a generous ellipse of skin is removed, they tend to recur. When the capsule is excised along with the tumor they quite as regularly do not recur. The recurrences grow more rapidly than the primary tumor and are much more prone to hemorrhage and ulceration. The recurrences are apt to be bosselated (Fig. 142). Secondary tumors are reported detached from the chief tumor. Some of these apparently are amelanotic melanomas. Recurrences are nearly always local. Metastases also have been reported. In such cases the diagnosis is in doubt.

Pathology. The striking feature is the attenuated skin covering the surface of the tumor. The line of demarcation between the tumor and the surrounding normal skin is sharp. When the surface ulcerates it usually involves the whole attenuated area. The recurrences are usually bosselated, but not always.

The tumors are very dense to the feel and give the impression of being attached only to the skin. On section the surface is seen to be made up of interlacing dense fibrous tissue. The tissue in some of them is so dense that the knife fairly creaks as the tumor is cut. In more rapidly growing recurrences this characteristic is lost, the surface being more uniform and pinkish in color.

When hemorrhage and ulceration occurs the exposed area is covered with blood clots and the underlying tumor tissue is softer.

Histology. The common microscopic picture is that of a moderately cellular fibroma or a very fibrous fibrosarcoma (*Insert*, Fig. 141). In the very slowly growing forms the fibre bundles are very heavy and almost devoid of cells. Even in these there are here and there more cellular areas. The recurrent forms are more cellular, being made up of fairly uniform spindle cells (*Insert*, Fig. 142).

Literature

Melanomas. The pigment finds its origin in certain cells situated beneath the epidermis. Do these belong to the epithelial cells or are they a special type of cell: that question has brought forth a whole literature. Demieville (Virchow's Arch., 1880, 81, 333) with much show of reason argued for perithelial and endothelial origin. Unna (Berlin. Klin. Woch., 1893, 30, 14; Histopath. der Hautkrank., Berlin, 1894, 1225) with equal ability and greater vehemence argued for their epithelial origin. He believes that all melanin-containing cells have a direct connection with the cutaneous epithelium, the hair follicles or ducts of sweat glands. Kromayer (Ziegler's Beiträge, 1897, 22, 412; Monatsch. f. Derm., 1905, 41, 477) on the other hand seems to have shown that nevus cells may participate in the formation of connective tissue. Judalewitch (Arch. f. Dermat., 1907, 58, 15) believes the epithelial cells become depigmented and are trans-

formed into fusiform cells. Ribbert (Ziegler's Beiträge, 1897, 21, 471) ascribes this formation to special cells, the chromatophores.

The site of production of melanin, despite extensive researches, still is a matter of doubt. Cowdry and Bloch (Special Cytology, Hoeber, 1919, I, 27) have recently published extensive summaries of the present day opinions. But their conclusions are of little aid to the surgeon. Cowdry accepts the general opinion that the chief site of melanin production is in the epidermal cells. He further states that "the second site of melanin formation is in the cells variously called Langhans cells, dendrite cells, melanoblasts, stellate cells, chromatophores which occur in the stratum germinativum." He regards them as functional adaptations of ordinary basal cells. Be this as it may, to the pathologist the conclusions of Mallory (Prin. of Path. Hist., Saunders, 1914, 341) are more acceptable. He believes it probable that the epithelial cells do not produce pigment but that the melanoblasts produce the pigment and transfer it to the epidermal cells. This view, he states, is proved by the fact that the cells of epidermoid cancers never produce pigment. This, I believe, warrants a separate classification for the melanin-containing tumors. Such a procedure is less confusing than the attempt to separate them into melano-carcinoma and melano-sarcoma.

Smith (Johns Hopkins Bull., 1925, 36, 185) recognizes two types of pigment cells. His observations are quite parallel with my own.

Fibrosarcomas of the Skin. The rather meager literature on these tumors may be set down as follows: in 1921 (Case Histories, Vol. II, p. 957, Mosby, St. Louis) I recorded several cases. In 1924 Darier (Ann. de Dermatol et Syph., 1924, 5, 545) described them under the name "dermatofibromes progressifs et recidivants." Willis (Ann. Surg., 1928, 87, 945) reports 2 cases and gives a good discussion of the histology. Senear, Andrews and Willis (Arch. of Derm. and Syph., 1928, 17, 821) report 2 additional cases. Willis quotes Hoffman (Dermatol. Ztschr., 1925, 43, 1). These authors emphasize the tendency to bosselation and even of multiplicity. This was not true of my cases. They were solitary until some cheerful person shelled them out. Several of the cases quoted resemble very closely the amelanotic melanomas of the spindle celled type to which they are, as above noted, very closely related.

PART II

CHAPTER VI

Malignant Tumors of Fascia

TUMORS of this group include those which lie between the skin and the bone. They lie over and between the muscles. Some of them, particularly the lipomas and myxomas may have no demonstrable attachment to the fascia. Many of the lipomas are obviously benign; others apparently benign recur and with each recurrence become more cellular and tend to develop a myxoid admixture which may ultimately become malignant. For clinical reasons these deeply lying lipomas should be regarded with suspicion. In contrast to these are tumors similarly located which are always malignant though the malignancy varies in the various locations. The basis of classification therefore, is clinical rather than histological.

LIPOMAS

As already noted some pure lipomas are included in this group because their topography is identical with those which tend to malignancy. Even of those apparently benign in structure in some the clinical course often belies their apparent innocent appearance. These tumors spring from the fascial planes of the muscles and from the connective tissue septa of the fatty layers. They are encapsulated, truly so in the histologically benign types, but imperfectly so in those tending to malignancy. There is no dividing line between the two. This fact makes it a clinical precept when excising deeply lying lipomas not to remove the tumors from their capsules but to excise the capsules along with the tumors even though it requires the removal of a layer of the adjacent muscle along with the tumor. The clinical importance of these tumors lies in this very fact. Many surgeons are impressed by the apparent complete encapsulation and remove the tumor from within this capsule. In the pure lipomas this in fact is sufficient but the gradation from the apparent pure lipomas to the myxolipomas, myxo-lipo-sarcomas and the pure

sarcomas is so gradual that no one can be sure with which he is dealing from the appearance at the operating table. Even the apparently pure lipomas, with the long finger-like interdigitations, must be carefully dissected out even to the smallest projections for if one of these is overlooked it may be the starting point of a recurrence which may ultimately result in malignancy.



FIG. 143. Lipomas of the abductor region. *A.* M., age 36. Lipoma in the abductor region many years. At operation it proved to be above the fascia but the fascia was in part defective. *B.* M., age 54. Came in for anal fistula. The lipoma in the upper abductor region was an incidental finding. It had a prolongation beneath the fascia.

The late Dr. Perkins once operated twelve times on the thigh of a woman which illustrated the progressive changes in these tumors. This patient alone furnished me class room material for the demonstration of pure lipomas, pure myxomas, and finally pure sarcomas obtained at the successive operations. This case represents well the general rule that these tumors show an increasing malignancy with each recurrence. The fate of the patient rests therefore in the understanding of the surgeon who operates the first time. This is even more true of those fascial tumors which are primarily fibrous, regarded as neurogenic by some writers. However, recurrences are not hopeless. I have repeatedly operated on

recurrences and secured permanent cures, even to 20 years. On the other hand the most painstaking primary operation will not cure the more malignant forms.



FIG. 144. Lipoma of popliteal space. M., age 49. Beginning as a tumor the size of a pea 30 years ago the tumor has grown to the size of a walnut. Three years ago it broke and ran a clear fluid. Since that time it has been covered by a scab. After the discharge it became softer and smaller. *Insert*, top view of same showing an ulceration in an area of attenuated skin.

Pathogenesis. There is no dividing line between the fascial and the subcutaneous lipomas. It is of interest to trace the various lipomas according to their topography. In some the relation to the fascia makes their benign character obvious (*A*, Fig. 143) because of its location above the fascia. Others again may appear to be above the fascia and yet may be but partly so (*B*, Fig. 143). In other cases the surface of the tumor may show a relationship to the skin sarcomas. These tumors are usually globular (Fig. 144), often somewhat sessilated. The surface is covered

with a thinned skin reddish in color and often it is defective at some point (*Insert*, Fig. 144). These are usually firmer and many of them deserve the designation fibro-lipoma. Some of these contain dilated lymphatics suggesting a relation to some forms of fibroma mollusca. The part of these tumors extending above the surface usually represents but a part



FIG. 145. Lipoma of the popliteal space a part of which is above but the larger part was beneath the popliteal fascia. The dome-shaped portion extended above the surface of the surrounding skin while the larger lower part occupied the popliteal space. Heavy bands of fibrous tissue divided it into lobules.

of the tumor. Quite commonly a large portion is subfascial and represents a deep lipoma (Fig. 145). This submerged part of the tumor is particularly apt to show myxoid areas.

On the other hand, deeply lying lipomas may have the same structure as the subcutaneous lipomas (Fig. 146). These are wholly innocent. Others again which lie deeply may show a mixture of myxoid tissue often with areas suggesting sarcoma. These are most commonly found in the popliteal space (Fig. 147) and in Scarpa's triangle, less often in the supraclav-

vicular fossa. In the supraclavicular fossa likewise lipomas are found presenting tumors of varying degrees of fibrous tissue admixture (Fig. 148) which may show recurrence after removal.

Pathology. The external form of the deeply lying lipomas is usually irregularly ovoid. The large size of the vessels in the capsule at once tells



FIG. 146. Deeply lying lipoma of the calf. F., age 58. Noticed tumor of the calf 3 years ago. Caused slight pain. *A*. The enlargement was dense, elastic on palpation. Positive diagnosis was not made. When the deep fascia was incised the tumor, *B*, popped out. In structure it is a pure lipoma.

the operator that he is not dealing with a simple lipoma and that capsule as well as tumor must be excised (Fig. 149). Pure lipomas do not differ in structure from subcutaneous lipomas. Deeply lying tumors seldom show such simple structure throughout. Usually there is an increase at least of the fibrous tissue (Fig. 145). Usually the cross-section shows a more pinkish or whitish appearance than an ordinary lipoma. The fibrous or

myxoid nature is usually obvious on inspection (Fig. 150). The various areas may present different consistencies. Fibrous areas may be quite firm, the myxoid areas soft, even semi-fluid. The formation of cysts is not unusual. These may be due to degeneration of myxoid areas or to hemorrhages into such myxoid areas. In some the extensive lymphatics seem to contribute to the cyst formation by adding to the degenerative



FIG. 147. Fibro-lipo-myxoma of the popliteal space. M., age 54. Swelling in popliteal space a number of years. Recently it became larger and painful. He was sent in to have an abscess drained. At operation the tumor was found to be fairly well walled off.

contents. In rare instances calcified areas are found. Degeneration may lead to the formation of large sacs which usually are filled with a straw-colored fluid; sometimes distinctly hemorrhagic and less commonly clotted blood is found. The wall of these cysts is thick and fibrous and sometimes neither lipoid nor myxoid cells can be found (Fig. 151). Despite the cellularity of the wall, wide excision is usually rewarded by a cure.

Histology. The structure of these tumors varies between pure lipoma and myxo-sarcoma. Often the tumors are not as malignant as one might



FIG. 148. Supraclavicular lipoma and a very malignant sarcoma. *A.* M., age 64. A week ago first noticed a tumor above the clavicle. It was the size of half a baseball. The larger part of the tumor dipped into the supraclavicular fossa. In structure it was a fibro-myxoma. *B.* M., age 23. Since a month ago he has noticed a tumor above the shoulder. He had a chill a few days ago. Since then he has been unable to sleep. Removal, rapid recurrence.



FIG. 149. Myxo-fibro-lipoma of the popliteal space. The tumor is pinkish white, the surface is slightly lobulated. In the capsule there is an abundance of large vessels.

judge from the microscopic picture. The lipoid and myxoid areas are classical and need no illustration here. The more cellular areas may cause apprehension. The cells may be uniform but more often vary in size and form. Usually in some areas the prolongations from the cells characteristic of myxoma can be found. So long as cells carry myxoid tails they can-



FIG. 150. Section of a myxo-fibro-lipoma of the popliteal space. The surface is pinkish white showing distinct bands of connective tissue everywhere in its surface. In the center is a degenerated area. The tumor did not recur.

not be very malignant no matter how fierce the nucleus may look (Fig. 152). If there is a tendency for the intercellular substance to liquefy it is additional testimony of benignity. In all such tumors there is a tendency to recur and with each recurrence they become more cellular and correspondingly more malignant. Therefore none of these tumors which show even a tendency to myxoid admixture should be unqualifiedly benign. As a surgeon he may hope, even feel confident, that they are clinically benign but as a pathologist he cannot admit it. Some of these tumors are

composed wholly of fibro-myxomatous tissue (Fig. 153) and it is only their location and gross appearance that suggests an alignment with the lipomas.

Some of these tumors may attain a considerable size before they produce a marked degree of protrusion (Fig. 146). This is due to the fact that



FIG. 151. Cystic degeneration of a myxolipoma of the thigh. M., age 35. One year ago had rheumatic pain in the left thigh. A tumor appeared. A. Fusiform enlargement of the thigh. B. Thick-walled cyst after removal. *Insert*, slide from the wall of the cyst.

they are held down by the deep fascia. Sometimes there is a history of a trauma following which the tumor appeared. This protrusion follows when the covering fascia ruptures. Because of the sudden appearance a diagnosis of muscle hernia is sometimes made. Because of the pain and fluctuant feel even abscess is sometimes suspected. Sometimes the history of trauma is lacking and the patient may state that no tumor was present before a recent date which may suggest a rapidly growing tumor. When the fascia over such large lipomas is severed they protrude of their own accord. This makes it obvious that they have been exerting pressure

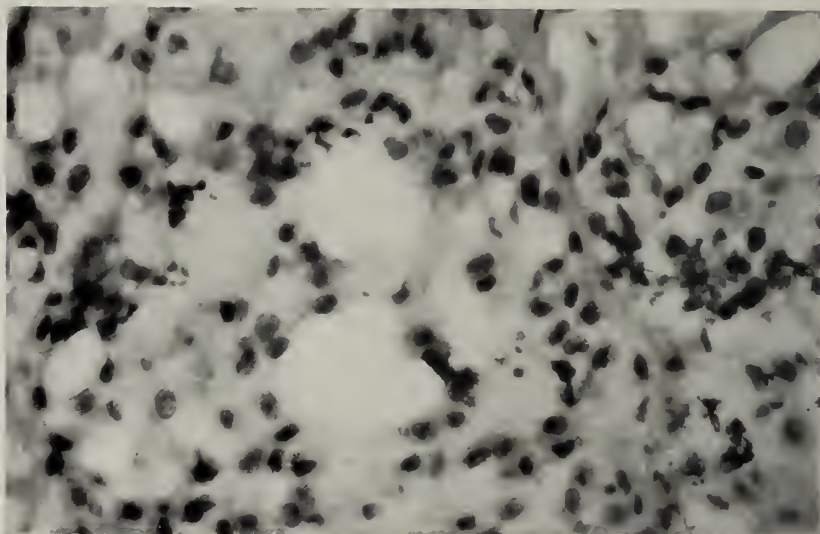


FIG. 152. Myxolipoma of the thigh. Large deeply staining cells are mixed with cells with lighter nuclei. The last named have prolongations which form more or less of a network. There are a few cells with large palely staining nuclei with deeply staining nucleoli. These are likely reticular cells. The tumor did not recur after removal.

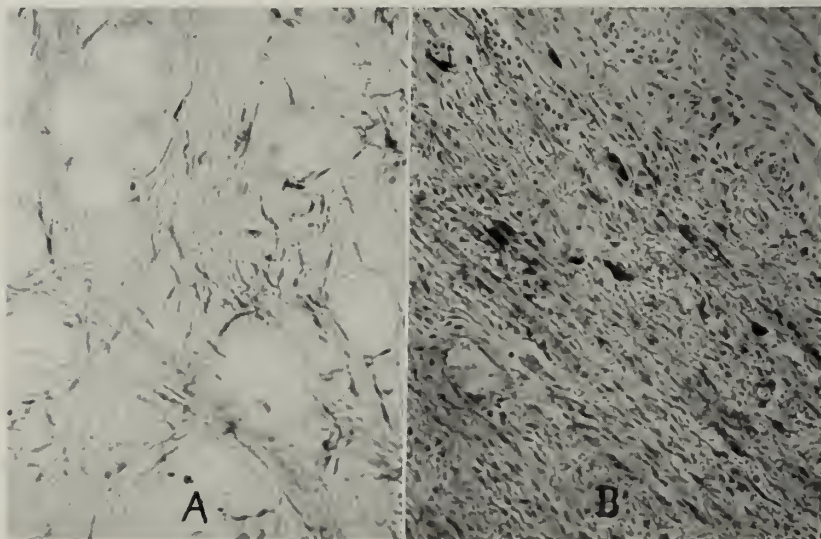


FIG. 153. Myxofibroma of the popliteal space. Tumor the size of a fist. *A*. The larger area of the tumor was made up of spindle and stellate cells with long interlacing processes. *B*. The minor part was made up of more or less dense areas composed of bundles interspersed with spindle form cells of varying size and stainability. The tumor did not recur.

beneath the fascia and it is easy to understand that after a time the fascia will yield to this pressure giving the patient the impression that he has recently acquired a tumor.

Tumors situated between the adductor group of muscles are particularly prone to send out long interdigitations between the muscles, even down to the sheaths of the larger vessels. This peculiarity of growth

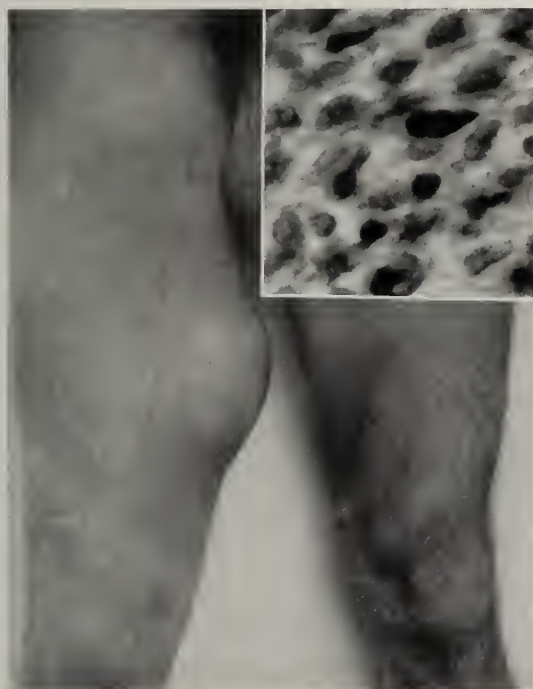


FIG. 154. Sarcoma of the medial side of the thigh. M., age 32. Struck on the thigh by a baseball 4 years ago. At the time of its removal it was as large as a grapefruit. Recurred in 6 months despite most radical removal. *Insert* shows why.

may make the operative removal a tedious affair since each process together with its sheath must be removed. In many of these cases a myxoid admixture is apparent at the operating table. In such cases the surgeon must realize that now or never the patient must be rescued for with each recurrence the tumor becomes more malignant.

SARCOMAS

The commonest of all tumors of the fascia are malignant from the beginning. They seldom justify so mild a term as "lipo-myxo-sarcoma" at any stage. They are pure sarcomas from the beginning. In a

few, however, the admixture of the cells suggests a possible previously more complex nature. These tumors are most common in the calf, the upper abductor region and in Scarpa's triangle in the lower extremity, while in the upper the bend of the elbow and the supraclavicular fossa are most commonly involved.

Pathogenesis. Topography is of great aid in evaluating the clinical disposition of the individual tumor just enumerated. Those of the calf are most often relatively hard, fibrous tumors but, despite their simple

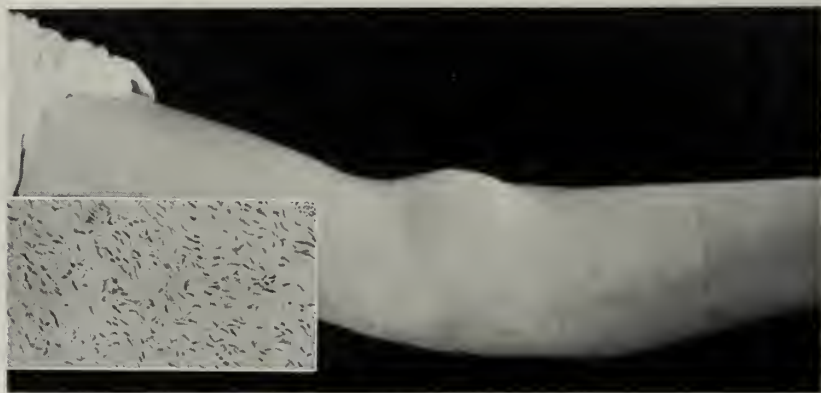


FIG. 155. Fascial sarcoma of the elbow. M., age 39. Four years ago noticed a painless tumor the size of a marble below the elbow. A year later it was removed. Two years later it recurred. It is now the size of an egg. Very radical operation was followed by recurrence. *Insert*, fibrosarcoma.

fibrous structure, they are prone to recur. These are close kin to some of the parosteal sarcomas and like bone tumors are prone to mediastinal and lung metastases. In such cases the secondary tumor may be discovered before the primary. I have seen one case each in which mediastinal and an intracranial tumor led to a successful search for a peripheral tumor.

Those tumors which lie distinctly in the adductor group of muscles may simulate the lipomas in that the patients often carry these for some years with no more serious consequences than mechanical interference with the various uses legs are put to. The vast majority however are firmer than the lipomas and grow more rapidly though, as previously mentioned, the history of sudden development in lipomas is not unusual. The location may be anywhere along the medial surface of the thigh (Fig. 154), curiously enough never on the lateral surface and rarely in front. Sometimes they follow trauma.

Fascial tumors about the clavicle are apt to be exceedingly malignant (B, Fig. 148). They simulate lipomas very closely and the history of onset is apt to be very misleading. Usually they have invaded the surrounding tissues when they first present themselves to the surgeon. This makes them easy to diagnose but it makes little difference to the patient for this type always ends fatally.

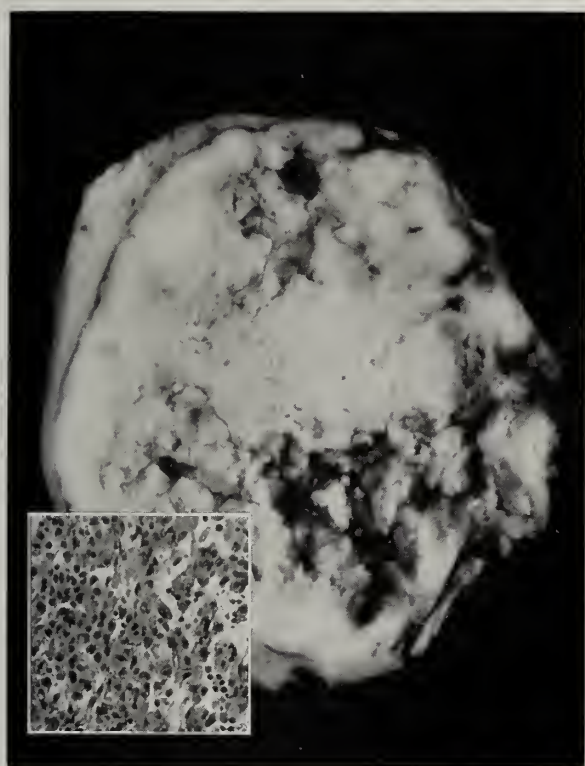


FIG. 156. Sarcoma of the abductor fascia. The tumor is spheroidal. At the left it has a well marked capsule. The mid-portion is in part broken down and on the right the capsule is destroyed. *Insert*, microscopic appearance of same.

Those lying in Scarpa's triangle are usually firmer from the beginning and generally are exceedingly malignant. Despite the most careful dissection at the first operation recurrence takes place in most cases.

In the upper extremity the problem is quite different. Here the tumors are usually denser to begin with and tend even more persistently to recur. Unfortunately this removal is usually first performed by those alien to the seriousness of the lesion. It is this group of tumors that one can most easily accept as neurogenic in origin though in the more rapidly

growing types they fulfill well the microscopic and clinical picture of a sarcoma, and it is well for the present to call them so.

Usually the topography and their density and spheroidal form first suggests a neurogenic origin for these tumors (Fig. 155). They are obviously deeply attached, never freely movable, but can be rolled from side to side with the deeper tissues. They recur promptly after removal in



FIG. 157. Sarcoma of Scarpa's triangle. The surface is fibrous and of a uniform consistency with but small softer areas at the upper right. *Insert*, the cells are dominantly spindleform.

most cases no matter how thorough the operation though the rate of growth varies much. Some require several years to finally reach the stage of inoperability. Others are softer in the beginning, grow much more rapidly, and soon form huge bosselated masses which tend to ulcerate.

In most cases it is the recurrence that brings the patient to the surgeon, the original tumor having been removed casually because it seemed to be completely encapsulated. It is local recurrence that first suggests the malignant character of the growth to the flippant operator.

Wide local growth followed by metastases in the lungs usually follow. Even wide excision of such local recurrences is followed by metastases, usually in the lungs.

Pathology. The tumors in the calf may be very hard, as firm as dense fibroids of the uterus, and may appear as innocent. Their appear-



FIG. 158. Fascial sarcoma of the shoulder. There is extensive hemorrhage in the center of the tumor and there is slight hemorrhage about the small lobulations. The soft tissues on the right are extensively invaded.

ance well suggests the term "recurrent fibroids" applied to them by the older writers.

Those situated in the abductor group of muscles are usually more or less soft tumors and may resemble the fascial lipomas just described. Despite the apparent innocent nature of the tumor as perceived through the intact skin, when exposed the deep prolongations along the intramuscular septae and the pinker color warn the surgeon that he is dealing with a tumor already malignant. They are not so simple as they look.

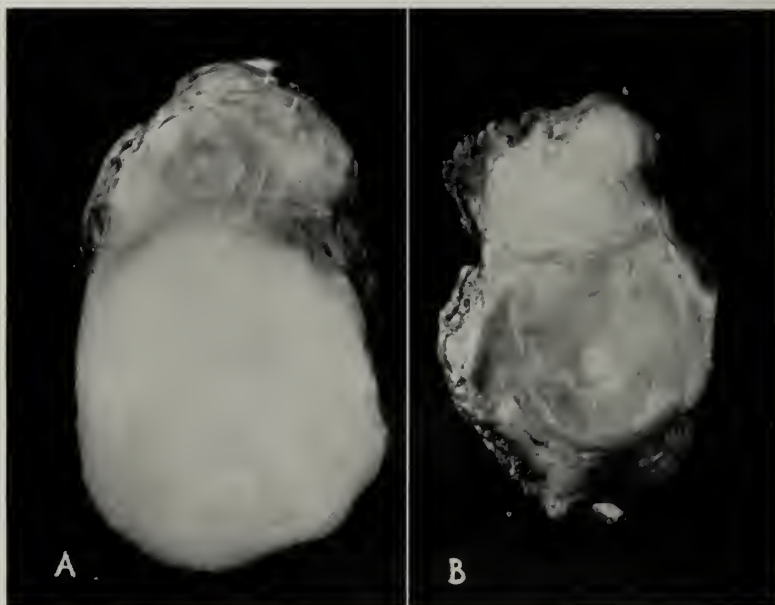


FIG. 159. Fascial sarcomas of the arm. *A*. Spheroidal tumor of uniform white color. The upper portion is pinkish and represents the new addition. *B*. A more rapidly growing tumor, showing pinkish softer areas.

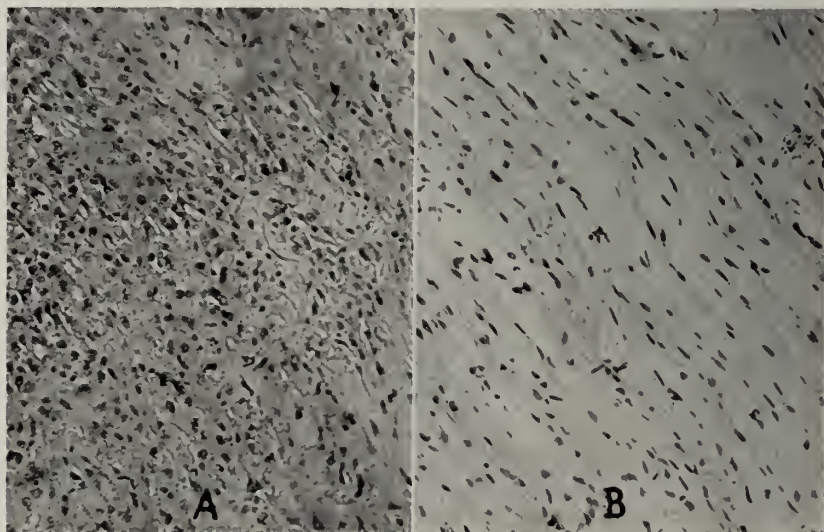


FIG. 160. Fascial fibrosarcoma of the calf. *A*. Very commonly these tumors have only small areas made up of such fairly cellular areas. Diligent search must sometimes be made for them. *B*. The bulk of the tumor is made up of closely placed fibre bundles with mostly small spindleform nuclei.

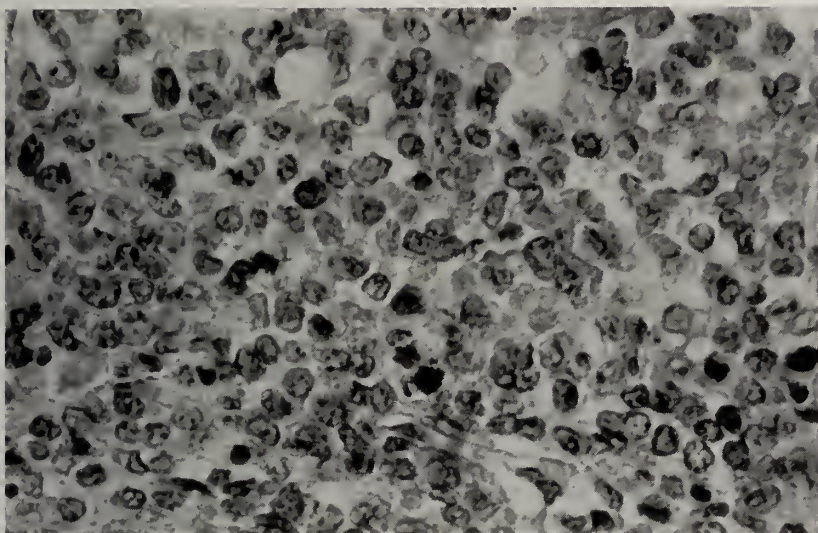


FIG. 161. Fascial sarcoma of the thigh. The dominant cell is spheroidal with a large granular nucleus with a prominent nucleolus. The cell protoplasm is not sharply defined. Small cells with deeply staining nuclei found here and there. The blood vessels are small, a number of which have their walls made up wholly or in part by tumor cells.

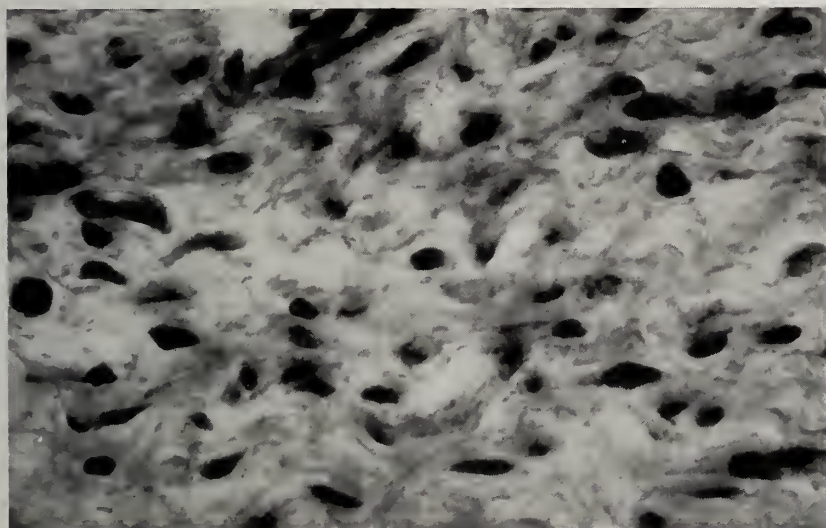


FIG. 162. Fascial sarcoma of the forearm. Fine wavy fibrils dominate the picture. The cells are spindleform and deeply staining for the most part. Occasional deeply staining spheroidal cells are scattered throughout the slide. Other parts of this tumor were more fibrous.

Those tumors which occur in Scarpa's triangle are still more malignant, firm, elastic. They are obviously fixed to a pseudo-capsule.

On section the dense ones of the calf cut hard and the surface is whitish pink, glistening and usually show the wavy parallel fibres. The sarcomatous tumors of the adductor group are usually spheroidal whitish pink, homogeneous unless marked by degenerative areas (Fig. 156). The tumors of the groin are usually distinctly ovoid with peripheral bosselations. The surface is usually homogeneous, whitish pink, but the color may vary giving the tumor a mottled appearance (Fig. 157). Areas of degeneration are not uncommon (Fig. 156). The very rapidly growing tumors may become hemorrhagic (Fig. 158). The hemorrhage and degeneration of the tumor may be so great that the cystic form of myxolipomas (Fig. 151) is suggested but their prompt recurrence and their excessively rapid growth soon dispels the delusion.

The more slowly growing tumors of the arm are distinctly whitish (*A*, Fig. 159) and sometimes show fibre bundles. The rapidly growing type are pinkish, bosselated and often show hemorrhagic areas (*B*, Fig. 159).

Histology. Histologically there are three dominating types of these tumors, the fibrous type of the calf, the cellular type of the thigh and Scarpa's triangle and the fibrocellular type of the arm.

The tumors of the calf frequently present a pure, very dense fibrous tissue. Usually they are fibrocellular (Fig. 160). The cell structure seems to have no influence on their disposition to recur and form metastases.

The fascial sarcomas of the thigh are usually more cellular in harmony with their more rapid growth. The dominant cell is spindleform, but it may be round and usually the two are more or less intermixed (Fig. 161).

The tumors of the arm are uniformly fibrocellular. Usually the fibres are fine and wavy. The cells are dominantly spindleform (Fig. 162) and are usually deeply staining. These tumors most likely are neurogenic (Compare *Insert*, Fig. 155). Much more rarely in the arm than these are the exceedingly malignant sarcomas which are altogether like those described in the thigh.

Literature

The literature bearing on these tumors is surprisingly meager. This may account for the mistreatment these tumors generally receive. Misjudged they make unattractive material for presentation in the press. A very notable exception to this statement is the paper of Seids and McGinnis (*Surg., Gynec. and Obst.*, 1927, 44, 232). To their excellent paper is appended a very full bibliography. Jaffe also (*Arch. Path. and Lab. Med.*, 1926, 1, 381) presents an excellent paper dealing more fully with the histological aspects of the border-line lipomas. This paper also contains a useful bibliography. Proescher and Meredith (*Surg., Gynec. and Obst.*, 1909, 9, 578) discuss the relation of cholesterolin to the myxo lipomas. The foreign literature contains a number of leading papers. Küttner (*Beitr. z. klin. Chir.*, 1929, 147, 151) discusses the deep lipomas, and Berard (*Lyon chir.*, 1929, 26, 629) the deep connective tissue tumors of the thigh.

CHAPTER VII

Diseases of the Muscles and Tendons

IT IS convenient to consider together the diseases of the muscles and tendons even though it does necessitate the discussion of very unlike conditions.

DISEASES OF MUSCLES

The diseases of the striated muscles do not comprise a very extensive group of diseases and their pathology is relatively simple. The chief are those due to inflammation of the connective tissue of the muscle bundles, which may be due to traumatism or to infection. These form the great group of myositis fibrosa. Specific infection, particularly syphilis and tuberculosis, may invade the muscle and excite reactive changes in the supporting tissue. Injury to the blood or nerve supply affects the structure in a manner which sometimes excites the interest of the surgeon. Invasion of tumor growth into muscle may excite a marked connective tissue reaction. The muscle changes associated with blunt trauma which are complicated by new formation of bone are discussed in the chapter on bone sarcoma in order to emphasize their clinical resemblance to bone tumors. The connective tissue reaction may give rise to definite tumors, often of keloid-like structure. The desmoids, a curious fibrotic reaction of distinct life history, rarely ending in sarcoma, are given separate consideration. Muscle hernias, not diseases of the muscle in fact but of the fascia covering them, may be placed here as a matter of convenience.

Traumatic Myositis (Myositis Fibrosa). The various myositides have been enumerated above. The range of possibilities is so great they cannot all be enumerated. One may say that the muscle may suffer from almost any disease of the skin above or the bone beneath all of which may in one way or another cause reaction on the part of the muscle.

Dull blows affecting muscles, particularly those lying over large bones, producing hemorrhages into the muscle with subsequent reaction on the part of the connective tissue form a most common group. Extravasation of blood with its subsequent absorption usually leaves but little trace. In more extensive hemorrhages the absorption may be tardy and a hematoma of long duration or even a cyst may result. In rare instances sarcoma in muscle may result from a single trauma. The production of bone,

the myositis ossificans traumatica (see volume on Diseases of the Bones) may follow injury to the muscle. Rupture of muscles from over-action, as in athletes, or from excessive action in convulsions, particularly in tetanus, belongs here as do lacerations of the sternomastoid during childbirth (Fig. 163). These are all followed by a myositis which may result in scar formation wider than necessary to repair the injury. Per-



FIG. 163. Myositis of sternomastoid. M., age 4 months—breach delivery. First noticed lump when 2 weeks old. Lump size hickory nut, rolls with sternomastoid. Resected. *Insert*, muscle fibres imbedded in much fibrous tissue.

haps also injuries from the injection of drugs, such as mercury and the various arsenical preparations, may as well be placed here. Aseptic operations on bones or even the muscles themselves may result in the formation of fibrous tissue.

Not all muscle injuries result in the development of clinically demonstrable myositis. In cases of lesser degree of injury the exudate is resorbed with little permanent injury to the muscle fibres. The extent of injury does not bear any direct relation to the extent of the fibrotic

change. In some cases a veritable keloid formation follows even after mild trauma (Fig. 164); invasion of the deeper tissues may produce extensive destruction of the muscle. On the other hand the fibrous tissue formation may be coextensive with the muscle injury. The result of



FIG. 164. Fibrosing myositis. F., age 23. Following vaccination the arm became enormously swollen with but little general reaction. Gradually subsided leaving fibrosed muscle. Slide shows fibrous tissue interspersed with more or less defective muscle bundles. *Insert*, microscopic structure shows dense keloid-like fibres.

the fibrosis is the destruction of the muscle fibres and because of this and the actual mechanical limitation by the fibrous tissue the function of the muscle is more or less destroyed. This condition follows injury to the blood supply either from the traumatism itself or by constriction of the bandage.

In many cases there is more or less production of new fibrous tissue with associated atrophy of the muscle fibres. In rare cases the muscle

fibres may be completely replaced by fibrous tissue. This is most commonly seen in poliomyelitis.

Pathology. The muscle bundles in some cases are seen at a glance to have lost their fullness and palpation reveals that what is left is dense and fibrous-like. The function of the muscle is lost. In other cases a circumscribed mass is hidden by the muscle and is apparent only on palpation.

On section early in the disease the muscle is whitish and edematous, sometimes with areas of infiltration of blood, even blood clots, but sur-

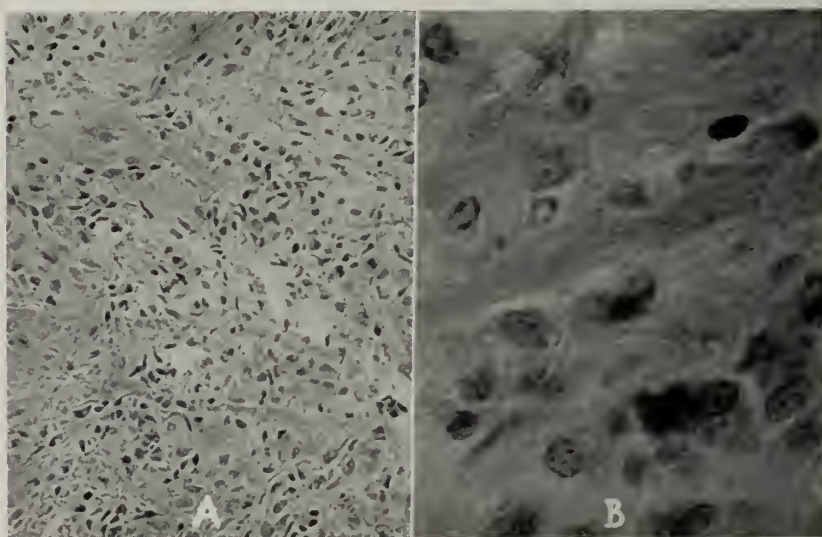


FIG. 165. Early stages of myositis. Ten days after injury diagnostic incision was made (in another clinic). *A*. Many large cells are interspersed between the palely staining muscle cells. *B*. High power of same. Large endothelioid cells, large nuclei with prominent nuclei. A muscle bundle runs through the middle of the field. Later, bone developed in this region and a typical myositis ossificans traumatica developed. Well after 12 years.

rounding the clot is always a margin of the white glistening edema. Later on the muscle bundles are pushed aside or interspersed with bundles of connective tissue. In terminal cases of extreme degree all appearance of muscle is lost and there remains but a dense keloid-like mass.

Histology. Early in the course of the disease an exudate with intermingling of leucocytes with or without a mixture of red corpuscles is all there is to be seen. Even so early the striae of the muscle fibres may be lost. This is followed in some cases by the appearance of large endothelioid cells which appear strikingly like endothelium (Fig. 165). Then follows a fibrosing stage which begins at the end of two or three weeks. The degree to which this progresses varies much. Usually remnants of

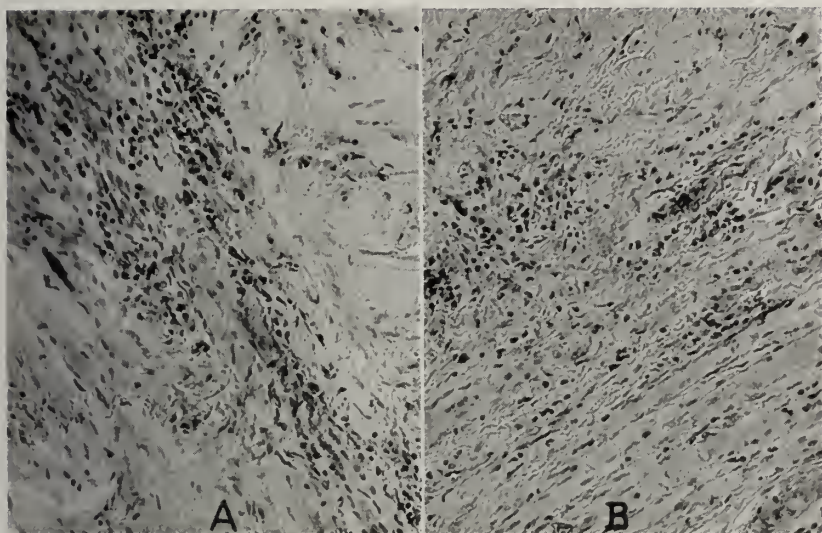


FIG. 166. Fibrosing myositis. *A*. Dense bundles of fibrous tissue are interspersed with more cellular connective tissue. The fibre bundles are heavy, dense, keloid-like, with sparse small spindle cells. *B*. High power of same. The dense keloid-like bundles above with fairly well preserved muscle fibres as the lower part of the cut.

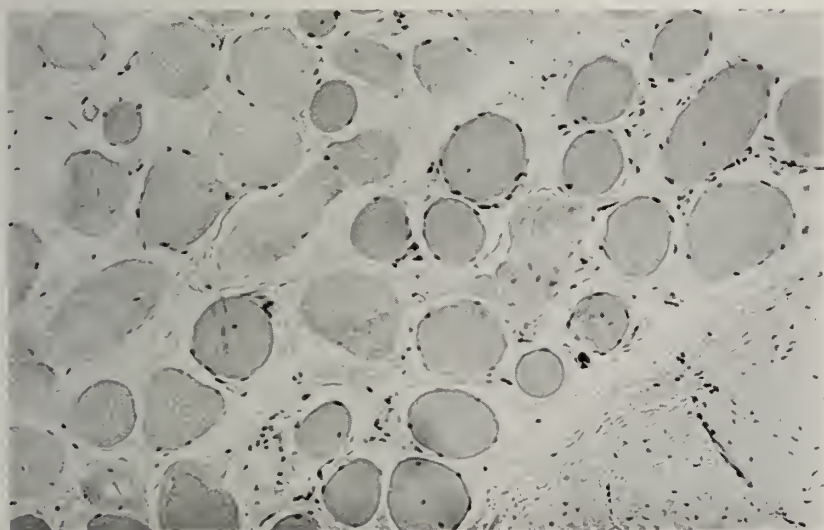


FIG. 167. Myositis of reaction and disuse. Area of muscle adjacent to old osteomyelitis followed by ankylosis. The muscle fibres are separated by loose connective tissue containing few cells. Muscle fibres palely staining; some of the fibres are atrophied and contain few nuclei. The striae are lost. Lower right, scar tissue.

muscle fibres are seen, the fibrous tissue lessening gradually near the periphery of the lesion. In extreme cases there remains but a dense fibrous tissue indistinguishable from keloid as seen in the skin (Fig. 166). In long past reactive processes, as after drainage of a chronic osteomyelitis, the muscle fibres are displaced by fibrous tissue (Fig. 167).

Infective Myositis. We are not concerned here with the generalized infections the result of constitutional diseases but only with those lesions due to local injuries. Muscles are singularly immune from infections,

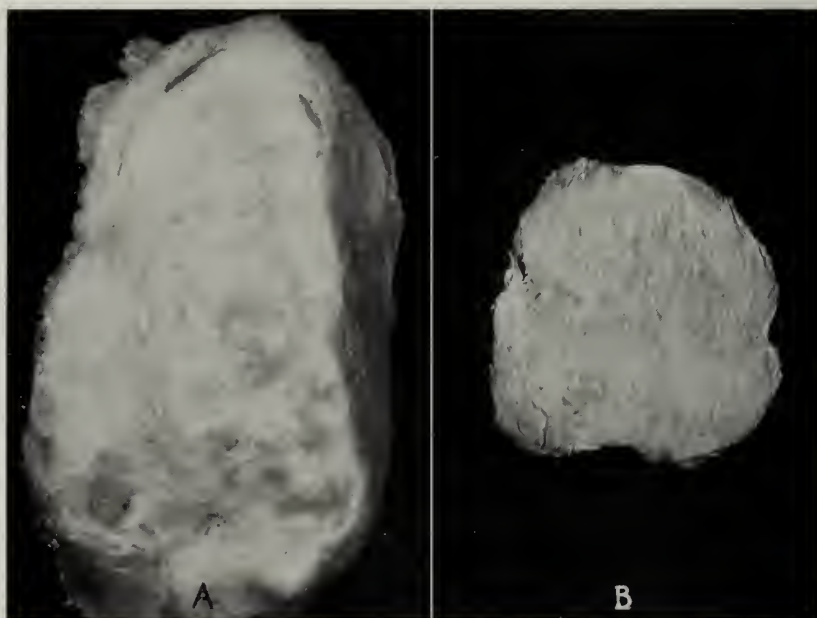


FIG. 168. Desmoids. *A*. Large densely fibrous tumor of pectoralis muscle. Whorls of fibrous tissue enclose more homogeneous areas. *B*. From rectus abdominalis. Dense fibrous tissue runs parallel through the tumor. No trace of muscle tissue remains.

which commonly follow fascial planes. Long continued suppuration of fascia is compatible with almost complete preservation of the integrity of the muscle fibres.

Pathogenesis. A great variety of conditions lead to infections of muscles. Injury of the muscle in operations for osteomyelitis, particularly of the humerus and femur, are the most common. Infections developing after the open reduction of fractures has added an amazing toll. Draining tracts as following tuberculous abscesses are followed by a limited myositis. Injections of drugs may add bacteria with the chemicals as irritants to the muscles.

The edema following infections is limited and is less dense than that involving the traumatic type just discussed and the recovery is usually more complete. Frank abscess formation within muscles is rare and involves the fascia more than the muscle.

The myositis following operative infection is often so diffuse as to destroy the function of the muscle. While muscle has an astonishingly rich plexus of capillaries the capacity for defensive reaction is not equal to the subcutaneous tissues. Often it is not alone the destruction of muscle substance that disturbs the function but the attachment of the fibrous tissue to bones or joints.

Sometimes following operations, as in herniotomies, there is a slowly developing infiltration, a veritable woody phlegmon, going on to resolution after six to twelve months without pus formation. These must be due to some bacterium of low virulence.

Pathology. The picture is usually comparable to that seen in the traumatic type but is more apt to be limited to the neighborhood of the infection. In severe infections the myositis is overshadowed by the infection which follows the fascial planes. Early there is not the increased firmness which characterizes the traumatic type of myositis and later the fibrous tissue formation is more limited, never producing a definitely circumscribed tumor as sometimes follows rupture of a muscle.

Histology. Polynuclear cells predominate in the early stages though later round cells are prominent. They are confined to the walls of the capillaries and do not infiltrate the entire field as they do in the non-infected variety. This explains the lesser tendency to scar formation in the infective type.

Volkman's Contracture. This is a variety of traumatic myositis which differs from both the preceding in its clinical significance and manner of its production. Thrombosis of the vessels rather than their rupture by a dull trauma is the irritating factor. This may be due to too tight bandaging but it should be remembered that the vessels may be injured by the original trauma. This is important in a medico-legal sense.

Pathogenesis. The primary changes are those due to the exudate which gives the muscle a firm feel. There is a loss of function first expressive of the edema, later of the fibrosis. Whole muscle bundles are prone to be affected tending to jeopardize the function of the entire extremity. Sometimes only a part of the muscle is affected. In some cases the limb is functionless due to fixation by newly formed fibrous tissue rather than the extensive destruction of the muscle fibres.

Pathology. In the beginning the muscle is swollen, the whole extremity livid. As the process continues resorption takes place and fibrosis begins leaving thin-bellied firm muscles interspersed with fibrous tissue. On section they are fibrous intermingled with bundles of preserved muscle. In extreme cases but little muscle can be seen.

Histology. In the early stages interfibrillary edema is the striking picture; this is replaced by a moderate cellular infiltration. The muscle fibres become smaller the result of malnutrition apparently rather than to reaction judging from the sparseness of the cell content which is made up largely of round cells.

Desmoids. These are more or less well defined tumors due to the proliferation of fibrous tissue which replaces the muscle fibres. The term is expressive of density.

Pathogenesis. These tumors are located usually in the abdominal muscles, most often the recti, less commonly the pectoral, and only rarely in other parts of the body. Muscle strain, as the expulsive efforts of labor, has been ascribed an etiological rôle. That this factor has been over-emphasized is evident by the fact that the condition occurs in spinsters and males. They are slowly developing tumors within the substance of the muscle. They shade gradually into the surrounding muscle though they may seem to have a pseudocapsule. They usually are flat and ovoid in outline and rarely exceed a size of 2x4x10 cm. but may be as large as a child's head. They commonly attain a certain size and then remain dormant for years. They may be attended by dull pain but quite as often are discovered by accident. In rare instance they become malignant, usually of a mild type and despite the sarcomatous nature of the neoplasm may still be curable by wide excision. Softness and rapidity of growth signalize the change in clinical character.

Pathology. They appear as very hard localized tumors not movable independent of the muscle. On section they are densely fibrous for the most part shading off rather sharply into the surrounding muscle (*A*, Fig. 168). The tumors may be intensely hard, showing only a fibrous structure without any indication of its muscle origin (*B*, Fig. 168). In some specimens the fibrous mass may still show some preserved muscle bundles and fibrous bands may be followed into the surrounding muscle. When they become malignant they are softer and pinker and the line between tumors and surrounding muscle is lost.

Histology. Dense fibrous tissue with small spindleform cells interspersed furnishes the microscopic picture. Usually muscle fibres are preserved throughout the tumor indicative of the perimysial origin of the

tumor fibres (Fig. 169). At the border of the tumor the fibrils of the tumor gradually lose themselves in the connective tissue of the muscle bundles (Fig. 169).

Metastatic Tumors in Muscles. Metastatic tumors in muscles may produce local swellings the nature of which is not always at once apparent. Round celled tumors may be confused with simple myositis. Im-

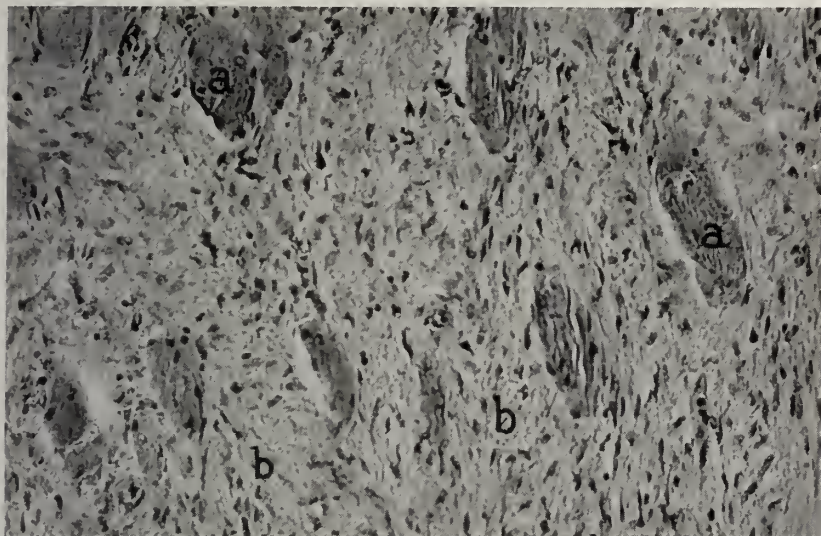


FIG. 169. Desmoid of pectoralis major: *a, a*, muscle fibres which have lost their striae and are split more or less longitudinally. They are identified more by their reaction to dyes than by their morphology. *b, b*. Dense, rather cellular connective tissue. The connective tissue is arranged in parallel bundles in part and in part in whorls.

properly removed sections for diagnosis are usually responsible for this confusion.

Pathogenesis. Secondary tumors in muscle usually extend by way of the lymphatics or directly through the connective tissue spaces. If the primary tumor be very small it may be overlooked.

Pathology. The section across a metastatic area usually makes the nature clear if it includes the tumor.

Histology. Even epithelial malignancies if the cells are few and isolated may simulate a myositis. Round celled tumors may be indistinguishable from myositis until the primary tumor is found.

Muscle Hernia. These are produced by a muscle belly protruding through a rent in the fascia.

Pathogenesis. Usually there is a violent trauma or excessive movement of the limb which tears the fascia permitting the muscle to bulge through the opening. It usually attains at once its maximum size. The



FIG. 170. Hernia of the biceps. M., age 52. A tumor appeared over the belly biceps during heavy lifting. Tumor subsides when muscle is relaxed.

biceps is most commonly involved (Fig. 170), the rectus femoris and the gastrocnemius less frequently.

Pathology. They are soft elastic tumors free from the skin. They are felt to harden when the muscle is caused to contract. Sometimes sub-fascial lipomas tear through the enclosing fascia and produce bulging tumors. These naturally do not contract. When exposed by incision of

the overlying soft parts normal muscle is seen to be protruding through a hole in the fascia.

Histology. In a recent case I once saw a mild myositis in the border of the protruding muscle. Long existing hernias may show a mild fibrosis.

Tubercular Myositis. Tuberculosis may cause inflammation indirectly by irritation from a pointing abscess or by the development of a tuberculous lesion within the muscle itself.

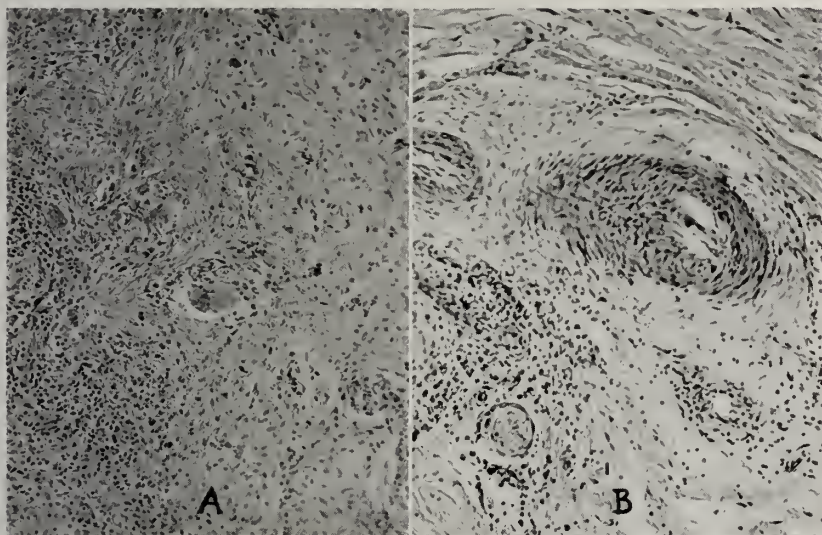


FIG. 171. Chronic myositis. *A*, tubercular myositis in a patient who had scrofula many years ago. *B*, syphilitic myositis; endarteritis with sclerosis about vessel.

Pathogenesis. Tuberculous myositis usually occurs secondary to a tuberculosis elsewhere as in the sternomastoid in cervical lymph gland infection or in the back muscles in spondylitis. The muscle lesion may first appear many years after the recovery from the primary lesion. It begins as a relatively painless thickening and goes on to sclerosis, seldom to the formation of a cold abscess.

Pathology. Aside from a location near a known tuberculous focus there is little to suggest its nature. When cut through the tissue has the appearance of a fibrosing myositis, seldom are there caseated areas.

Histology. The picture is that of a chronic fibrosing tuberculosis. The fibrous tissue dominates the picture more than in most tuberculous lesions (*A*, Fig. 171). Definite tubercles and giant cells may be absent.

Syphilitic Myositis. Syphilitic myositis may be diffuse or, which is the most common, localized—the gummatous. The diffuse may occur in the secondary stage. The localized, the gummatous type, only in late syphilis.

Pathogenesis. I have seen gumma in the following locations: the lower end of the sternomastoid, the tongue, the pectoral, quadriceps femoris and the external sphincter of the anus. The trapezius also is a frequent site but almost any muscle may be affected. It begins as a more or less circumscribed nodule, most often the size of a hickory nut. The



FIG. 172. Chronic tenosynovitis. M., age 69. Painful swelling on dorsum of right hand. Thickened, baggy, very tender to pressure. Gradually subsided over several months.

pain is usually moderate but may be acute. After a period of months they break down and if they reach the surface the defect in the skin is reniform.

The diffuse syphilitic myositis is characterized by moderate pain, both spontaneous and on movement. It tends to progress to fibrosis without breaking down.

Pathology. The early gumma has the feel of a hematoma but is generally more circumscribed. On section the ovoid form and the degenerated center is readily recognized. The diffused form presents the characteristics of a diffuse myositis without anything to distinguish it from like affections of the muscle due to general diseases.

Histology. The structure of the gumma is distinctive but the diffuse form has only the vessel sclerosis to suggest its nature (B, Fig. 171).

DISEASES OF THE TENDON SHEATHS

Aside from the acute tenosynovitis common after unusual strain, less common after injury, which rapidly recovers with rest and consequently yields no tissue for histological study, there is the chronic infective variety and the more serious tuberculosis of the tendon sheaths. Cysts and tumors make up the balance of the more common diseases of the tendons.

Chronic Infective Tenosynovitis. Little has been written about this disease likely because no one is certain as to its nature. In times past I have treated these as tuberculosis and prided myself on the excellent results obtained. During the past ten years I have seen a number which run a very definite subacute course terminating in recovery.

Pathogenesis. The wrist, or both wrists simultaneously or in sequence, are most commonly affected, much less common on the tendons of the foot. More or less suddenly the wrist swells producing a fusiform swelling (Fig. 172) which is excessively painful. There is commonly an attending elevation of temperature to 102° or thereabout with general constitutional reaction. The inflammation progresses to recovery after many months. I have seen it most commonly in persons well past middle life. Occasionally they continue indefinitely with little change but with gradually diminishing pain, and increasing firmness of the affected region. After the disease has existed for a certain length of time there is a rarefaction of the bone which disappears when the tendon affection recovers and the function of the joint is resumed.

Pathology. The affected part is spindleform, but very tender to the touch in the early stages. The patient is apprehensive of pain before the manipulation begins. As the disease progresses the firmness increases but never exceeds a stage of more or less boggy. As the disease recovers the firmness lessens. When cut into the synovial sheath is seen to be much thickened and the peritenon tissue is edematous from a glary translucent exudate. The tendon is not changed nor is there an excessive fluid within the sheath. The tendon sheath is affected for a greater length than is the case of either tuberculosis or gonorrheal tenosynovitis by masses of uniform red granulation tissue. There are no gray granulations often seen in tubercular tenosynovitis.

Histology. In the earlier cases the edematous tissue is infiltrated with polynuclear and round cells. In cases of longer standing there is marked thickening of the vessel walls and the peritenon tissue is made up of round cells producing a veritable granuloma. No free pus is formed. Bacterial studies have been inconclusive.

Tubercular Tenosynovitis. In contrast with the preceding the tubercular variety is slower of onset and is less likely to be painful. Spontaneous cure on the other hand is unusual.

Pathogenesis. The tendon sheath infection is usually secondary to a lung focus though often enough this is not discovered until the tendinous involvement is obvious. Often the disease exists for a considerable period

without pain. When the median nerve becomes involved there may be numbness, tingling, even severe pain. The swelling is gradual, limited in extent in the beginning but later may extend, in the case of the wrist from the mid-forearm to well into the palm. When the primary focus is in the finger, the synovial sac of which does not connect with the palm, it may remain localized here indefinitely (Fig. 173). As the disease progresses the swelling increases which may remain as a fusiform swelling (Fig. 174) but if there is an increase of exudation within the sheath a more



FIG. 173. Tubercular tenosynovitis of middle finger. M., age 40. Had tubercular testis removed. Fusiform swelling of palm, baggy, semi-fluctuating. Contained rice bodies. Died of lung tuberculosis.

localized bulging, particularly in the palm of the hand, may be manifest. When the bulging is localized in the lower forearm sarcoma is not infrequently suspected. The tendons are spared for a long time, even years. When there has been a considerable fluid within the sheath precipitation in the fluid may take place producing the so-called rice bodies. After a considerable time, many months at least, there may be a regression of the process with ultimate healing, particularly if the process is confined to one finger. Usually sooner or later the tendons are attacked and it is common to find one or more destroyed. The disease may invade the joint or the skin and a discharging sinus may result with subsequent mixed infection. Sometimes the perforation is anticipated by some unwary attendant. In such cases the reaction may be very severe demanding amputation. The whole picture may be complicated by a more or less advanced pulmonary tuberculosis.

Pathology. Early there is a boggy swelling relatively painless to manipulation. The swelling may be loculated, particularly in the palm of the hand when there is one protruding mass below and one above the anterior annular ligament. The various lobules may differ in contents, the one containing clear or straw-colored, thin, or more or less gelatinous contents while its neighbor may be filled with rice bodies. There may be a sense of fluctuation and after the rice bodies form these may be



FIG. 174. Tuberculosis of tendon sheath. F., age 36. Lung tuberculosis several years. Wrist swollen nine months. Tumor elastic. Mass involving flexor tendons of wrist. Dissected free. Recovery. *Insert*, slide of same, showing typical tubercles and giant cells.

indefinitely felt as small flat bodies which glide about under the examining finger. When cut into the peritenon tissue is typical of tuberculosis, grayish white interspersed with redder granulation tissue. The tendons except in the earliest cases are yellowish or grayish. The tendons may be matted together at the most severely involved areas. In advanced cases the various tendons may be united by fibrous tissue making their separation difficult. There may be a considerable exudate within the sheath. In old cases the rice bodies may be present which have been likened to melon seeds, more or less flat bodies of yellowish white color, smooth of surface, firm of consistency and of a homogeneous texture.

They are by no means characteristic of tubercular disease out of chronic bursitis since they are found in mucous bursae, particularly in those about the knee joint. They are likely due to coagulation of albuminous substance.

Histology. The structure is typical tubercular granulation tissue, giant cells and all (*Insert*, Fig. 174), though about the border of the lesion considerable areas may be found made up of granulation tissue without definite evidence of tuberculosis. This must be remembered when the



FIG. 175. Ganglion extensor tendon. M., age 26. Tense smooth swelling over extensor tendon. Smooth-walled sac containing synovial fluid.

exact source of the tissue submitted for examination is not known. As in joint tuberculosis the demonstration of tubercle bacilli in the section is notoriously difficult. In cases in which the histological picture is inconclusive the guinea pig may give positive evidence.

Ganglion. These are cysts attached to or bulging from synovial sheaths. They occur most commonly on the extensor tendons of the hand and the dorsum of the foot.

Pathogenesis. They appear as smooth round nodules over the body of a tendon. They are frequently attended by pain particularly in the beginning giving basis for the theory that muscle strain has something to do with their genesis. Once fully developed they seldom cause inconvenience to those insusceptible to the cosmetic appearance of their hands. They sometimes disappear spontaneously. The older surgeons antici-

pated this by striking them a hard blow with the family hymn book. When caused to disappear by this means they commonly returned.

Pathology. These tumors are smooth, tense, movable only as the tendon sheath is movable (Fig. 175). When exposed they are dome-shaped and glistening. They contain a thick clear glary fluid. When this escapes there remains but a translucent sac. It is seldom possible to remove them without permitting the escape of their contents and exposing the underlying tendon.



FIG. 176. Xanthoma of ring finger. F., age 60. Gradually developing lump on finger 7 years. Operation showed extensive attachment on all the tendons of the finger.

Histology. The wall is made up of palely staining fibrous tissue containing few very small nuclei. The cysts are lined with flat endothelium. In the outer wall of the cyst are many small blood vessels.

Giant Cell Sarcoma of the Tendon Sheaths (Xanthoma). Though tumors of this character are found elsewhere in the body those of the greatest clinical importance occur about the tendon sheaths and aponeurosis, most commonly of the hand. They may be associated with bursae and sometimes in the subcutaneous tissue independent of any joint structure.



FIG. 177. Giant celled sarcoma of the tendon sheath. Multiple primary tumors. Besides the larger tumor at the joint small nodules are shown to the right and left of it. The small tumor shows a cross-section of the main tumor.



FIG. 178. Xanthoma of elbow. M., age 60. For some years has been developing knots on both elbows. Painless, smooth, firm, elastic. Slide shows xanthoma.

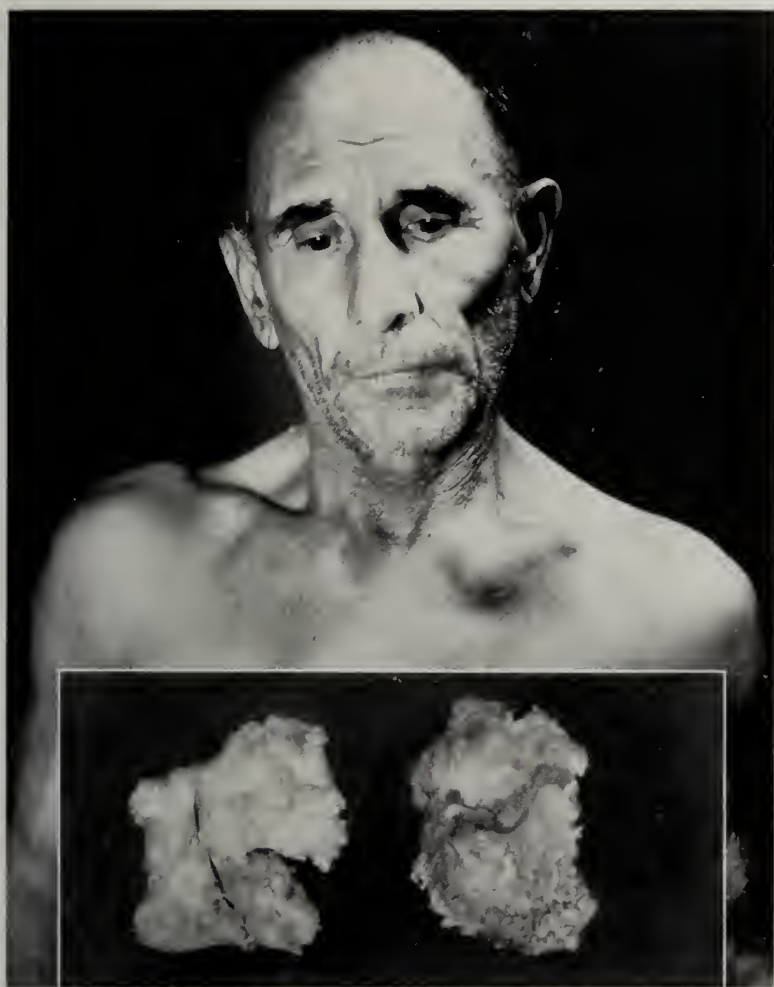


FIG. 179. Xanthoma of sternoclavicular joint. M., age 65. Swelling size egg. Some tender recently. *Insert*, joint capsule much thickened. Shows typical xanthoma and giant cells.

Pathogenesis. They begin as small nodules, most commonly near a joint. These increase in size until they reach that of a hickory nut or a walnut, seldom larger. They do not limit the function of the part and are painless. After they attain a certain size they remain stationary for an indefinite period though some tend slowly to advance. They rarely show malignant tendencies unless inadequately removed and at worst they show but a feeble malignancy by persistent recurrence. Metastases

are said not to occur. They form globular tumors free from the skin but loosely or more firmly attached to the tissues beneath (Fig. 176). They appear well walled from the surrounding soft parts but the apparent encapsulation is deceptive. The capsule must be removed along with the tumor or recurrence may take place, particularly in young patients and tumors that are growing. Neither the joint surface nor the tendon is destroyed but in some cases their removal requires such extensive exposure of tendons and joints that amputation is advisable. They may

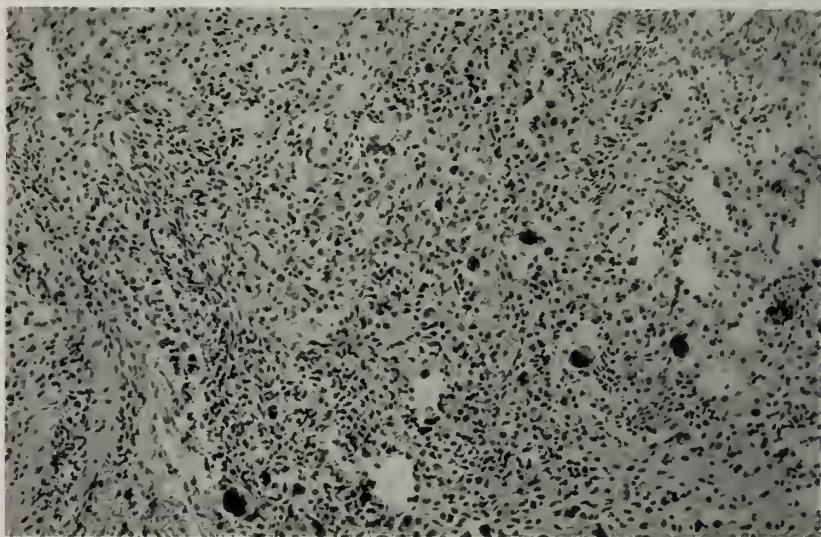


FIG. 180. Xanthoma of the tendon sheath, from a recurrence. The dominant cell type is spindleform and polyhedral. The giant cells are small, the vessels relatively numerous and large. Xanthoma cells are absent.

become multiple after inadequate removal or they may be so from the beginning (Fig. 177).

These tumors may spring from any tendon or joint surface or from the periosteum at a distance from a joint (Fig. 178). They may occur in other situations the result likely of constitutional conditions. Though like in name and structure to these tumors they are of no surgical significance.

Tumors of like structure not uncommonly involve the sterno-clavicular joint (Fig. 179). They form enlargements of the joints, developing slowly and painlessly and recurrence does not follow excision.

Pathology. The ovoid, sometimes bosselated masses are firm, slightly elastic to the touch and quite painless. When cut across they are grayish

white with yellowish areas of greater or less extent (*Insert*, Fig. 181). The more rapidly growing ones may be a uniform pale pink. The joint and tendon surfaces are not involved and the overlying soft parts are respected but extension to the skin may take place particularly after incomplete removal. Those occurring in bursae may be firmly attached to the underlying periosteum.

Histology. The essential structure is fibrocellular within which are multiple giant cells with uniformly distributed nuclei (Fig. 180). The

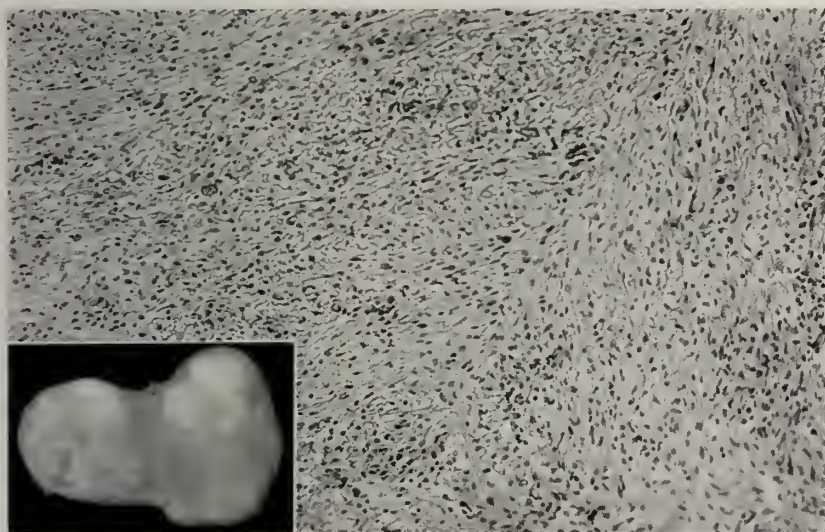


FIG. 181. Xanthoma of the tendon sheath of the dorsum of the foot. The dominant cell is spindleform enclosing within their meshes numerous xanthoma cells. *Insert*, gross section showing yellowish areas in the bosselations.

essential cells are spindle and polyhedral surrounded by bands of connective tissue. The abundance of cells often leads to needless apprehension for they may simulate sarcoma, particularly when the giant cells are absent. In some tumors the dominant cell is distinctly fibrillar (Fig. 181). In such cases the location of the tumor (*Insert*, Fig. 181) and the presence of xanthoma cells are distinctive. The xanthoma cells are large cells containing lipid material. These cells may be so abundant as to impart a yellowish appearance to the gross specimen. They are not an essential part of the tumor. The giant cells likewise may contain lipid material and while usually present in large numbers may be sparse or absent in large areas. They sometimes contain pigment in the protoplasm. Those of more rapid growth show an increase of the cells particularly of

the polyhedral cells. Recurrences and metastases may lose all trace of the original tumor and appear as a very cellular sarcoma.

Rare Tumors of the Tendon Sheaths. A variety of tumors occasionally are found attached to or developing from the tendon sheaths. Chondromas are usually confined to the sheaths of the tendons of the fingers. They may become calcified. Lipomas either inside or outside of the sheaths are somewhat more common. These do not differ in pathogenesis or structure from similar tumors occurring in the joints. They occur



FIG. 182. Dupuytren's contraction. M., age 78. No disturbance since he does not work. Also has induration of penis.

most commonly in the palms of the hands. Here they may cause marked bulging of the palm. Sarcomas of the tendon sheaths are rare. They begin as metastases. My case recurred after extensive removal and despite amputation metastases in the lungs speedily formed. Tumors of the tendon proper have not been reported. In one of my cases calcium deposit followed injury. This was at first thought to be bone.

Dupuytren's Contracture. This condition is a dense fibrosis of the peritenon tissue of the flexora of the hand involving particularly the fourth and fifth fingers. It occurs chiefly in advanced life and is of unknown etiology.

Pathogenesis. The onset is gradual. A thickening under the skin of the palm is first observed. As this increases the extension of the finger

is interfered with (Fig. 182). Trauma is often blamed but true Dupuytren's contracture must be differentiated from scar formation due to gross injury such as burns of the palm and synovial sheath infection. As a result of the contracture the function of the hand may be much interfered with.

Pathology. The dense fibrous ridge which is intensified when the affected hand is passively extended reveals the whole pathological picture. When cut into the knife grates as the parts are severed. The cut surface is smooth glistening. The tendons are not infected.

Histology. The finer structure of the tissue is that of dense fibrous tissue quite like keloid. The reticular layer of the corium is most extensively involved. The walls of the small vessels may be much thickened.

Literature

The literature on the diseases of the muscles and tendon sheaths is recent and abundant and is particularly well represented in our own literature.

Tumors of Muscles. Mason (Ann. Surg., 1930, 92, 444) contributes a report on 50 cases of desmoids and appends an adequate literature. Wolbach (Arch. Path., 1928, 5, 775) and also Hirsch (Arch. Path., 1929, 8, 9) have written about rhabdomyomas of muscles. The former (Anat. Record, 1928, 37, 255) in a separate paper enters into a detailed discussion of the development of the myofibrils in these tumors. Davis and Kitlowski (Arch. Surg., 1928, 20, 39) contribute a paper on intermuscular hemangioma. An extensive review on circumscribed ossifying myositis is presented by Liebig (Erg. d. Chir. u. Orth., 1929, 22, 501) in a paper of 83 pages. Chambers (Arch. Surg., 1928, 16, 755) reports an unusual case.

Inflammation of Tendon Sheaths. Kanavel (Surg., Gynec., and Obst., 1923, 37, 635) reports 14 cases of tuberculosis. Winterstein (Erg. d. Chir. u. Orth., 1930, 23, 151) writes on tendon sheath stenosis; Breuer (Arch. f. klin. Chir., 1926, 141, 754) on non-specific inflammations of the tendon sheath.

Tumors of the Tendon Sheaths. Buxton (Brit. J. Surg., 1923, x, 469) gives a classification and discusses chondromas. Strauss (Surg., Gynec. and Obst., 1922, 35, 161) was able to collect 18 cases of lipomas. Janik (Ann. Surg., 1927, 85, 897) reports 2 cases of chondroma and has collected 7 other cases. He believes irritation or injury precedes the development of the tumors and regards them as granulomas. He finds only 70 cases of myeloma.

Myeloma (Xanthoma). Broders (Collected Papers, Mayo Clinic, 1919, 11, 1032) reports 17 cases. Stewart and Flint (Brit. Jour. Surg., 1915, 3, 90) present a good summary and append an excellent bibliography. McWhorter and Weeks (Surg., Gynec., and Obst., 1925, 40, 199) report a case of multiple xanthoma and discuss the literature.

Sarcoma. Krogius (Acta chirurg. Scand., 1922, 55, 363) reports a case of spindle celled sarcoma with recurrence.

Dupuytren's Contracture. Kanavel, Koch and Mason (Surg., Gynec. and Obst., 1929, 48, 145) present a masterly résumé of the subject together with a short bibliography of the noted surgeons who first satisfactorily described the disease in 1852). They mention trauma, constitutional state and heredity as possible etiological factors. One of my patients had also sclerosis of the penis. They also discuss the pathology. Koch (Am. Jour. Surg., 1930, 9, 413) writes on the acquired contractures of the hand.

PART III

CHAPTER VIII

Neoplastic Diseases of the Blood and Lymph Vessels

THIS chapter has to do with the tumor-like affections of the blood and lymph vessels. It is often difficult to say whether there is a simple dilatation, a developmental anomaly of the vessels, or a tumefaction due to some reactive process either in normal or abnormal vessels, usually the latter, or finally whether a tumor is the result of newly formed vessels. Only the last named are true neoplasms.

In practice it is convenient to consider these together because they are not always separable, the one merging into the other. The diseases of the two classes of vessels must be considered separately. The following classification is well adapted to the clinic:

- Hemangiomas
 - Capillary Angiomas
 - Venous Angiomas
 - Cavernous Angiomas
- Lymphangiomas
 - Simple Lymphangiomas
 - Cystic Lymphangiomas
 - Cavernous Lymphangiomas

As a corollary to these diseases elephantiasis may be considered because it is due to disturbances in the lymph or venous circulation.

HEMANGIOMAS

These tumors, as the name implies, are the product of blood vessels. Strictly speaking only tumors the product of newly formed vessels should be included. This would exclude all varicosities whether acquired or due to developmental anomalies. It likewise excludes tumors in which increase in the connective tissue is the dominant factor,

such as exuberant granulation tissue, very vascular sarcomas and the endotheliomas. The surgeon cannot hold to such a strict interpretation of the term. To him a hemangioma is a tumor made up chiefly of blood vessels. Most of them are really developmental anomalies either unchanged or complicated by reactive processes. It is often difficult to say how much newly formed vessels have to do with the increase in size



FIG. 183. Hemangioma of the face and lip. M., age 26. Capillary angioma of the face, venous angioma of the lip.

of the tumor. In those rare cases in which there is undoubtedly proliferation of the vessels, usually it is evident that the connective tissue assumes the initiative and the vessels but scramble to keep up the pace. The clinical behavior of such processes may vary from innocent exuberant granulations to the most malignant sarcomas.

At the same time it must be remembered that true tumors the product of newly formed blood vessels do occur. Some declare their neoplastic nature by forming metastases. These tumors, however, are so rare that they concern only the pathologists and these controversial points do not

concern the practicing surgeon. He can take them as he finds them without much concern as to their genesis.

Therefore in conformity to the practice of most authors, we may divide the hemangiomas into three groups: first, the capillary; second, the venous angiomas, and third, the cavernous. Obviously the terms express only degrees of comparison. There is no sharply defined line between them but the separation has certain advantages for purposes of clinical recording. The vascular nevi should not be included with the angiomas, no

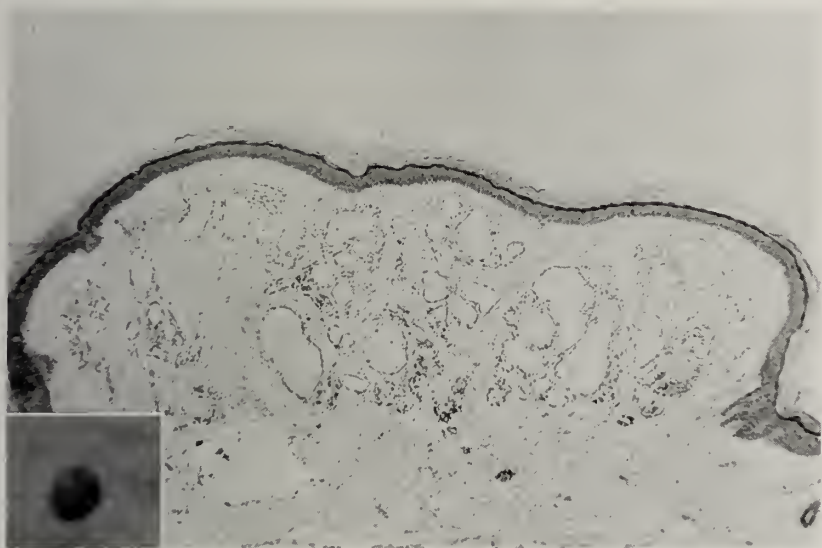


FIG. 184. Capillary angioma of the face. The epidermis is unchanged. The superficial capillaries are dilated endothelial lined spaces without definite walls. *Insert* shows relation to surrounding skin.

matter what the prominence of the blood vessels, for in them the nevus cells are the dominant factor, not the blood vessels.

Capillary Angiomas. These are intradermal capillary varicosities for the most part and are represented by the port wine birthmarks seen soon after birth.

Pathogenesis. These lesions appear shortly after birth and soon assume their fully developed forms. They are obviously congenital anomalies. They vary from the size of a pin-point to large areas covering a considerable part of the face (Fig. 183 and *A*, Fig. 186) or of some other part of the body. They are chiefly of interest because of their cosmetic relations. They may be associated with the deeper types of vascular diseases.

Pathology. The deep red color disappears on pressure. When the capillary dilatation is marked they may be palpable as slight elevations above the surface of the surrounding skin (*Insert*, Fig. 184). When the blood escapes the discoloration disappears.

Histology. The slide shows only dilated cutaneous capillaries lined with endothelium, but devoid of perivascular cells which differentiates them from vascular nevi (Fig. 184). When associated with venous angiomas their direct relation with the subcutaneous vessels is evident.

Venous Angiomas (Arterio-Venous Hemangiomas). This type is represented by the common elevated birthmarks. They appear as more



FIG. 185. Hemangioma of nose. M., age 3. Compressible, becomes distended when the child cries. Relieved by mass ligation.

or less circumscribed protuberances of reddish or reddish-blue color. They may present mere points soon after birth and enlarge during the first months, though some do not appear until some months or years later. Or they may consist of protuberant masses as large as half an apple, ovoid or irregular in shape. The common sites are about the nose, cheeks, forehead, neck and scalp, but they may occur on any part of the body. They are more deeply seated than the capillary type and may be covered more or less by normal skin. A part of the surface may be covered by a smooth white area of skin suggesting a scar. Usually at the highest point of the tumor the skin is involved by the superficial vessels.

Pathogenesis. The lesion, if present at birth, may disappear, but more commonly it increases in size proportionate to the growth of the child. In rare instances they grow rapidly and according to the literature occasionally show malignancy. Not infrequently melanotic tumors contain dilated vessels but these should not be classed with the angiomas.

These may become malignant but it is the melanotic part of the tumor that becomes destructive and not the blood vessels; they perform in every way as melanotic tumors.

When angiomas increase in size they may develop pulsation or tributary arteries may be palpated at some point on the periphery. Com-



FIG. 186. Hemangiomas of various typical regions; *A*, of face and temple; *B*, over the great fontanelle; *C*, infraorbital region; *D*, above ear.

pression of these arteries may cause decrease in size of the tumor. The larger examples of this condition have received much discussion in the literature under the caption of arteriovenous aneurysms. The difference is chiefly one of size. All have abundant communication with the adjacent venous system which unite into more or less isolated vessels which seem to invite ligation by the surgeon.



FIG. 187. Hemangioma of buttock. Large lobulated compressible tumor of the buttocks present at birth. F., age 3. It must have had wide connections with the deeper vessels because it was easily compressed with the flat hand but instantly returned when the pressure was removed.



FIG. 188. Angioma of cheek. F., age 9 months. Large globular, partly compressible mass. Partly reduced by radium.



FIG. 189. Large hemangioma of temporal and frontal region extending to orbit. M., age 7. Death from air embolism during attempt at removal. The veins of the tumor were connected with those of the dura by vessels 3 to 5 mm. in diameter. These connecting vessels were very numerous.



FIG. 190. Venous angioma of scrotum. M., age 26. Large conglomeration of veins covering scrotum and perineal region extending well over buttocks. Relief by ligation and excision. The connecting vessels with the deep pelvic vessels were very large and thin walled making operation difficult.

As the tumor increases in size the skin covering the summit may become thinned to the point where spontaneous rupture occurs causing alarming hemorrhage or rupture may be caused by injury or injudicious treatment, particularly by escharotic pastes used in the attempts to obliterate the underlying vessels.

These tumors are usually symptomless and may reach a point where increase in size is no longer noted. In fact, the general tendency is to decrease in size as the child grows older. Usually, because of their prominence and unsightly appearance, they are subject to treatment and



FIG. 191. Hemangioma of forearm and hand. M., age 14. Large conglomeration of veins of palm and back of hand producing marked disturbance in the closing of the hand. Relieved by ligation.

it is only in patients residing in the wide open spaces that one may observe their normal life history.

They are most commonly situated over the tip of the nose (Fig. 185), over the great fontanelle (*B*, Fig. 186), at the side or root of the nose (*C*, Fig. 186), above the ear (*D*, Fig. 186), but are common at other regions of the face and neck, and about the buttocks (Fig. 187).

The deeper type may involve the superficial vessels also (Fig. 188) or may involve wide areas of the subcutaneous vessels without involving the skin (Fig. 189). Those on the scalp may have wide communications with the intracranial vessels making their removal hazardous from thrombosis or air embolism. The skin veins as well as the deeper ones may be involved (Fig. 190). Involvement of deep veins of hand (Fig. 191) or foot may cause impairment of function by displacing the tendons or by involvement of the muscles. They may lie below the fascia and extend widely into the muscle (Fig. 192).

Pathology. These tumors are soft to the touch and compressible but become more tense when the child cries or the affected part is made pendant. Fibrous tumors may cause areas of greater firmness. After the removal of the tumor the blood escapes and the tumor collapses and shrinks. The cut surface is grayish-white but yellowish areas are some-



FIG. 192. Hemangioma of the temporal muscle. M., age 46. Tissues above fascia not involved. Partly relieved by excision.

times seen. When the blood has coagulated before the removal of the tumor the surface may be a deep bluish color (Fig. 193), usually traversed by the fibrous septa. That in such cases the blood does not really escape proves their relative independence of the surrounding circulation. When carefully dissected out and ligated a conglomeration of vessels is demonstrable (Fig. 194).

Histology. Escape of the blood causes the vessels to collapse and their endothelium to appear higher so that the vessels come to resemble

glands (Fig. 195) and not infrequently are mistaken for sweat gland adenomas. Some of the spaces retain blood and thus their nature is made obvious (Fig. 196). The covering epidermis may be much attenuated. The connective tissue may be cellular, and with the marked diminution of the lumina of the vessels, appears to make up a large part of the field, so much so that the beginner may think of a sarcoma (Fig. 197). The intravascular cellular tissue is particularly pronounced in those covered by papillary keratotic epidermis. Notwithstanding the size of the vessels

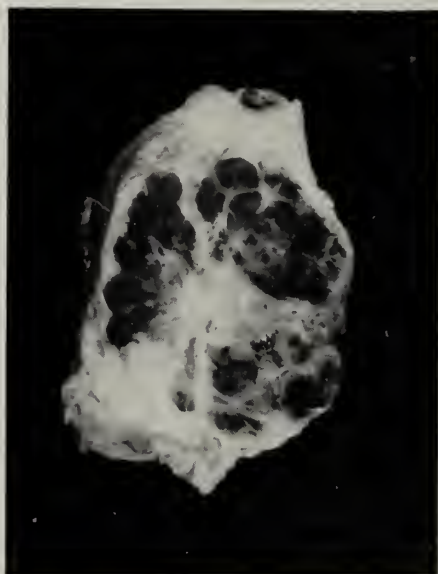


FIG. 193. Hemangioma of infraclavicular region. M., age 5 months. Complete excision and fixation before sectioning. Dark areas are the blood spaces filled with blood clots.

these tumors bear a closer relation to the melanomas than to blood vessel tumors. When such tumors become malignant the nevus cells cause the mischief despite their sparseness (Fig. 198). The blood vessels have been wrongly blamed. Malignant angiomas have been reported, and no doubt do occur, but a close study of the cell type must be made before metastases can be accepted as the product of vascular endothelium.

Cavernous Angiomas. These differ from the preceding in that the blood-containing spaces are larger, more irregular, and lack the definite walls of fully-formed blood vessels. They are congenital anomalies; spaces that had failed to form normal blood vessels.

The common site is the tongue, neck and axillary region (Fig. 199). They begin, or at least are first observed, in early life and commonly do

not undergo further development after puberty. There may be a number of intercommunicating cavities which may or may not have communication with the blood stream. These are merely endothelial-lined cavities filled with blood.

Pathogenesis. Though their congenital origin cannot be proved in many cases, their occurrence in early childhood, their occasional appearance in several members of a family, and their close resemblance to the



FIG. 194. Large angioma of the forehead after removal by ligation and dissection. The mass is made up of a conglomeration of large veins.

lymph cysts, which are commonly observed in the same region, leave no choice but to accept this explanation as to their origin. The skin covering them is unchanged.

They may develop slowly or remain stationary. When the blood within them coagulates the wall becomes irritated to which the surrounding connective tissue reacts producing pain and rapid enlargement. The skin may become involved and, it is said, perforate and cause alarming hemorrhages; though search of the literature fails to disclose a single satisfactory recorded case. When the tumors spontaneously regress this reaction with coagulation evidently brings it about.

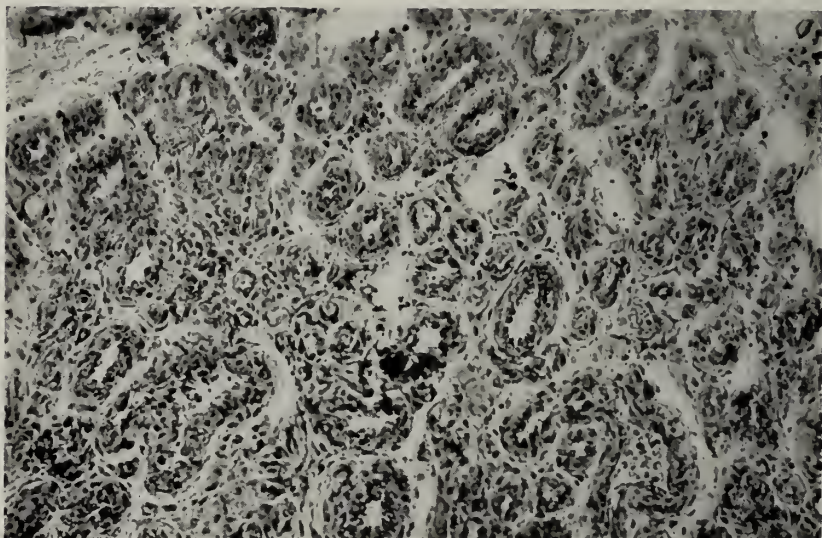


FIG. 195. Superficial angioma of the face. When emptied of blood the vessel walls contracted causing the endothelium to pile up high thus imitating a sweat gland adenoma. The perivascular connective tissue is unusually cellular, the nuclei large and deeply staining.



FIG. 196. Hemangioma of the scalp of a child. The vessels are filled with coagulated blood: *a*, large vessel with a very thin wall, *b*; at the left is an area of relatively acellular connective tissue. Such thin walled vessels when emptied may appear as mere clefts in the tissue.

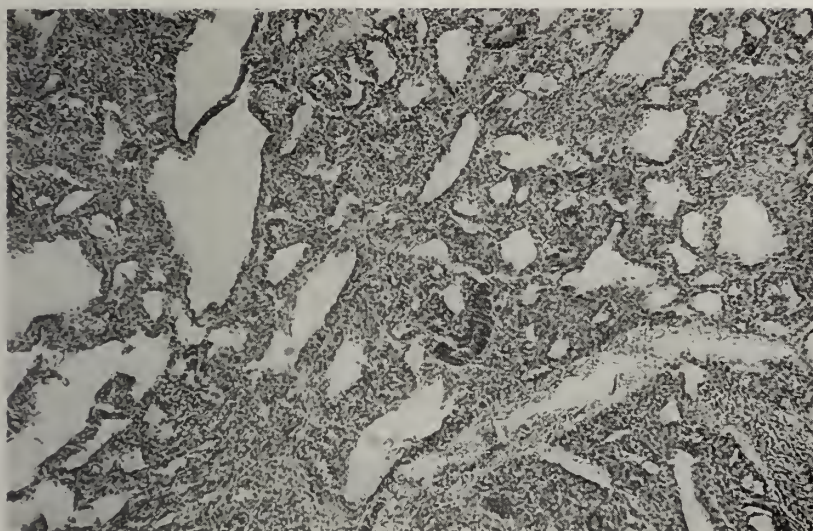


FIG. 197. Hemangioma of the scalp of a child. The vessels are large endothelial lined spaces without definite walls. The intravascular tissue is made up of large deeply staining cells with little intercellular connective tissue. Such a tumor may suggest a so-called "angiosarcoma."

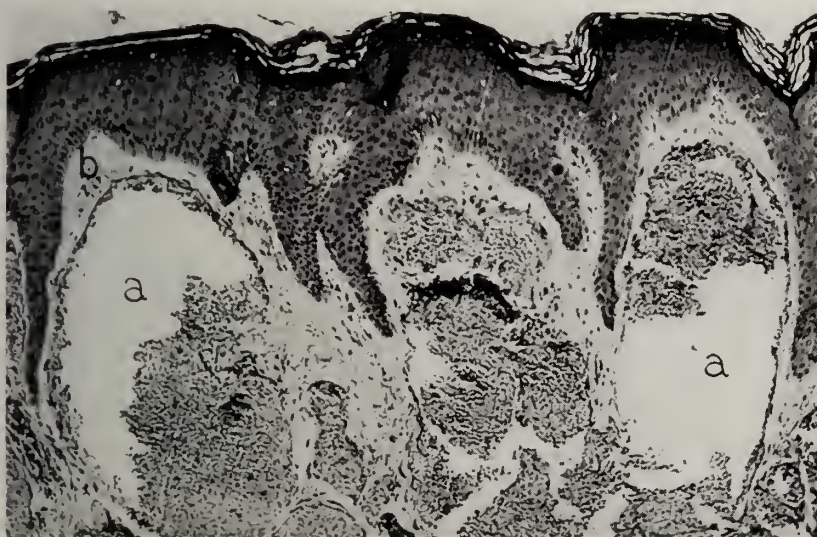


FIG. 198. Papillary angioma of the temple. The epidermis is thickened, the surface keratotic; *a*, large venous spaces partly filled with blood; *b*, small group of nevoid cells. These tumors are congenital. When they become malignant it is the epithelial cells that cause the mischief.

Pathology. The tumors are elastic and fluctuating, or when they lie more deeply, semi-fluctuating resembling the feel of a myxoma or lipoma. When they have communication with the blood vessels they are compressible. When hardened specimens are cut across they are seen to be made up of smooth-walled sinuses or the walls may be covered with clots in various stages. Plaques of calcification or considerable thickness



FIG. 199. Cavernous angioma of the tongue and neck. F., age 10. *A*. The left half of the tongue is much thickened; *B*, the parotid region, the neck, and suprasternal notch show dilated vessels.

of fibrous tissue may be found but walls of the sinuses are usually thin and lined with endothelial cells.

Histology. In those cases in which reaction has occurred changes incident to such complications are in evidence. There may be a considerable number of fibroblasts about the capsule which sometimes intrigues the examiner into diagnosing a true neoplastic process.

LYMPHANGIOMAS

Lymphangiomas are developmental anomalies comparable with like lesions of the blood vessels. Unlike similar tumors of the blood-vascular system, however, a direct connection with their circulatory system can seldom be demonstrated. Like the blood vessel tumors, it is advan-

tageous clinically to separate them into anatomic groups between which there is no dividing line.

Lymphangiomas are of interest because their development is associated with distinct reaction in the peri-vascular connective tissue albeit this reaction is due most likely to primary changes of the lymph. Because of these periodic inflammations the tumor increases in size and takes on distinct neoplastic properties.

Conditions due simply to an occlusion of the central channel have often been classed with lymph tumors but without justification. Chronic edemas following acute inflammation, elephantiasis of whatever origin and the like have been so classed. But these belong in the same category



FIG. 200. Cystic lymphangioma of the perineal region. It is made up of a conglomeration of pea-sized cysts lying within the skin and movable with it.

as varicosities and will be considered under the general head of elephantiasis.

Certain congenital lesions, like macrocheilia, macroglossia, macro-melia, represent dilated congenital lymph channels and the terms have but a topographic significance. These are often associated with the more pronounced tumors commonest about the neck supraclavicular and axillary regions. The large cavernous tumors in which septa have been destroyed producing one or more large cavities are designated lymph cysts.

Though the lymph tumors are less sharply divided than like tumors of the blood vessels there is a clinical advantage in dividing them into groups. The simple lymphangiomas corresponding to the capillary angiomas; the cystic, comparable with venous angiomas; and the cavernous, which correspond very closely to the tumors of blood vessels of like designation.

Simple Lymphangiomas. These involve only the dermal and subcutaneous lymphatics and are freely movable with the skin over the underlying fascia. They are local blemishes rather than serious diseases and as such have been much classified and subdivided by the dermatologists.

Pathogenesis. Being congenital, pathogenesis can but record the changes they undergo during the lifetime of the patient. The simple lymphangiomas are represented by small tumors of from miliary size to elevated irregularly shaped tumors (Fig. 200), reaching, in rare instances,



FIG. 201. Lymphangioma of thigh located in Scarpa's triangle. F., age 26. Numerous cysts occupying the skin and subcutaneous tissue limited by the deep fascia.

the size of the palm or even larger. They are most common about the buttocks and thighs. They tend to remain stationary but may develop by the addition of other spaces about their periphery. They cause no inconvenience except from their size. When situated on the tongue because of their tendency to increase in size after each period of reaction they become very serious maladies, in rare instances terminating in malignancy.

Pathology. The smaller lymphangiomas appear as single vesicles which stand out from the surface of the skin like newly formed blisters. The larger ones likewise appear as superficial vesicles of variable size, irregular of contour and shading without definite outline into the surrounding skin (Fig. 201). The vesicles being tense the lesion is firm to the touch corresponding to the size and number of vesicles rather than to the amount of connective tissue between them. When in a state of reaction the pericystic induration adds to the mass of the tumor. In this way a

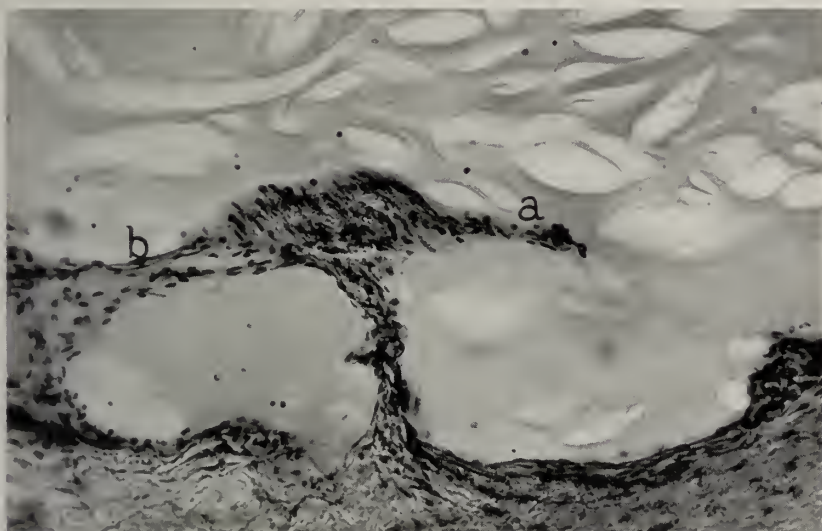


FIG. 202. Lymphangioma of the forearm. Small cyst and another which has ruptured into the larger cyst: *a*, incomplete wall; *b*, complete wall. Cysts are lined with flat endothelium.

mass may be produced involving the skin and subcutaneous tissues as large and thick as a hand.

When the recently removed tumor is cut across the contents escape and the tumor collapses in proportion to the degree that the cysts bear to the tumor as a whole. If fixed before they are cut the lymph is coagu-



FIG. 203. Lymphangioma of the lips. *A*, M., age 15. Lower lip has been enlarged since infancy. No complaints. Wedgeshaped excision. Cured now 20 years. *B*, Dilated lymphatics following injury.

lated and the cyst spaces appear as whitish or translucent spheroidal areas lying in a background of connective tissue.

Histology. The slide shows the small spheroidal cysts lined with a low flat endothelium. Only rarely is the endothelium elevated (Fig. 202). Between the cysts are lymph spaces in which the endothelium may be higher and show evidences of the formation of new lymph spaces though such pictures are less common in this type than in the group next to be considered.

Cystic Lymphangiomas. The more deeply lying tumors, because of the larger size of the individual compartments warrant the term "cystic." There is no definite dividing line between this form and the simple



FIG. 204. Lymphangioma of tongue. M., age 14. Tongue has been inflamed at intervals of six months for several years. Mass occupied right half of the tongue for two inches. Small clear cysts cover surface of tongue (*insert*). Excision. Cured 16 years.

type just described. These are usually entirely subcutaneous, lying beneath the skin, sometimes within and between the muscles, but they may be associated with the superficial variety just described. When confined to special regions they may conveniently be designated by indicative terms such as macrocheilia, macromelia, macroglossia, etc. Modesty apparently has prevented the application of the same principle to like affections when they occur in the genital region.

Pathogenesis. The slighter forms are seen in the lip where the tumors are made up of dilated lymph spaces enlarging the region as a whole (Fig. 203). These are of consequence to no one except the patient. The commonest type involves the submaxillary region, the axillary region, and are sometimes associated with like lesions in the neck. These are large, sometimes huge and their compartments are large which warrants classifying them as cavernous.

This type of lymphangiomas takes on special significance when the lymphatics of the muscles are involved, particularly so when the lymphatics of the tongue (Fig. 204) and the extremities are affected (Fig. 205). Repeated inflammations in these regions cause the tumors to increase in size, gradually destroying the muscle fibres and causing their replacement by fibrous tissue. That it is not due to any properties of the muscles



FIG. 205 .Lymph cysts involving forearm and hand causing deformity. Cysts extended between muscles and tendons. Laborious dissection secured only partial correction.

is obvious since the same changes occur in lymph tumors of the subcutaneous tissue, notably the cheek and neck.

These striking reactive changes consist of periodic inflammations in the connective tissue about the cysts. Following trauma or without known cause, the affected part becomes inflamed resulting in marked increase in size and density. Pain and constitutional reaction are severe in proportion. I have seen temperatures to 105° F. with delirium in a boy of 4 during intense reaction in a lymphangioma of the calf (Fig. 206). The process runs its course in from ten days to a number of weeks. The important clinical fact is that the lesion does not return to its former size but always remains somewhat larger. This increase in size seems to be

due, as indicated above, to the occlusion of neighboring lymphatics and formation of new cysts as well as new lymph spaces. It is this tendency to react that gives these tumors their clinical dignity. Those cysts associated with well formed lymph follicles are the most apt to undergo reactive changes. This is of importance when the lesion is situated in the tongue. Here these periodic reactions lead to the enlargement of the tongue until the mouth is no longer able to contain the organ. I was once able to follow such a case over a period of ten years, the patient's parents persistently refusing operation while the child and the lesion were both small. By the time the lad attained his eighteenth year the mouth could



FIG. 206. Lymphangioma of calf. M., age 4. In state of reaction following therapeutic application of X-ray. Excision, recurrence, mid-thigh amputation. Death in nine months from lung metastases. *Insert:* Type of cells which made up the tumor.

no longer contain the tongue which made it obligatory to remove the entire organ whereas a resection of a small part of the tongue would have sufficed early in the course of the disease.

The cause of the reaction about these tumors is not known. Since no bacteria are present it is fair to assume that it is due to some reaction, perhaps clotting of the lymph within the lymph cysts. A similar process occurs about blood cysts.

When the same condition develops in an extremity the results are not so disastrous since usually it terminates in but an inconvenient enlargement of the limb. However, two serious complications may take place. The extension may reach to the hand or foot (Fig. 205), seriously impairing its function, or very rarely a malignant condition may be implanted on the lymphangioma. I have seen one such case in a boy aged four. Following a series of X-ray treatments applied with the idea of obliterating the

lymph spaces an intense reaction followed which never subsided and terminated in a sarcoma which even amputation did not halt (Fig. 206).

When lymph tumors of the neck become inflamed the swelling may be so intense as to embarrass respiration so that a tracheotomy may be required. Save for the history of a preceding tumor when in a state of



FIG. 207. Cystic lymphangioma of the submaxillary region. M., age 14. He had a soft flabby mass under his left lower jaw since childhood. Some weeks ago without known cause it became hard, hot, and painful and he had a fever. It formed a hard semi-edematous mass firmly fixed to the deeper tissues. The reaction subsided in six weeks, but remained larger than before the inflammation began.

reaction a Ludwig's angina may be suspected (Fig. 207). This is a grave error for incision into them is inevitably followed by annoying lymph drainage which becomes infected with embarrassing, even serious results.

The lymph cysts likewise may provide interesting superficial complications. The surface skin may become perforated by the course of the disease or by accident and a continuous serous discharge take place. This is always annoying and may become exhausting from the loss of lymph and the cyst itself may become secondarily infected.

Pathology. Cystic lymphangiomas may appear as spherical nodules elevating the skin. The connective tissue between the cysts may be so abundant that, associated with the tense cysts, a fairly firm mass is produced. The tumor is more impressive to touch than to sight.

Deeply lying lymph tumors are soft, semi-fluctuating, often slightly compressible. When not attached to the skin they may resemble lipomas especially when situated within the muscle, notably in the adductor region of the thigh or in the calf. Usually the history of early origin is

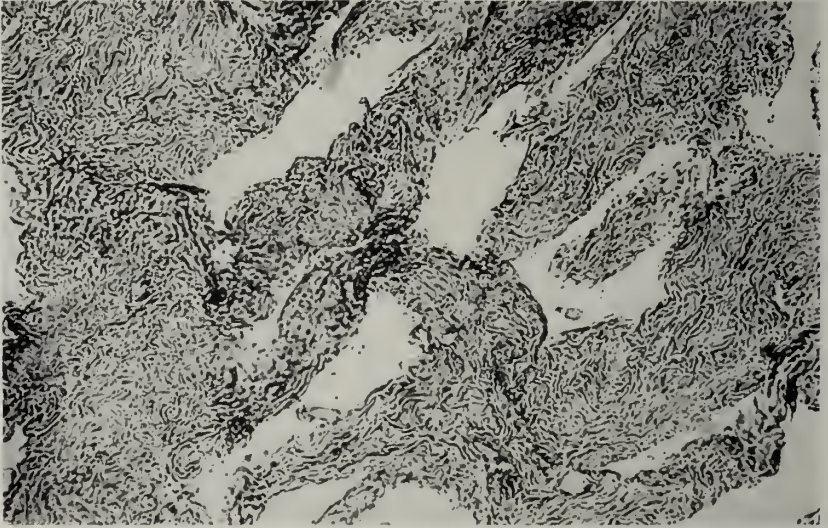


FIG. 208. Lymphangioma of the lip. The lymph spaces are collapsed leaving only irregular endothelial cell lined clefts. The intercystic connective tissue contains few cells.

distinctive but in the locations just mentioned the previous existence may have escaped notice. Once reaction has taken place firmer areas remain. This may not be apparent in the more deeply seated tumors but is pronounced when the lesion is in the tongue. Here the affected part is felt to be hard. The individual cysts are felt as shot-like tumors when the tongue is grasped between the thumb and finger though the tongue may look normal on inspection. In some cases the small cysts are so near the surface that they may be readily seen (Fig. 204).

On section, the tumors after removal, like blood vessel tumors, are a disappointment since they collapse; there but remains a small flabby fibrous mass representing, after the escape of the lymph, but a small part of the original tumor. When tumors are in reaction or after a series of exacerbations the connective tissue is so much increased that a con-

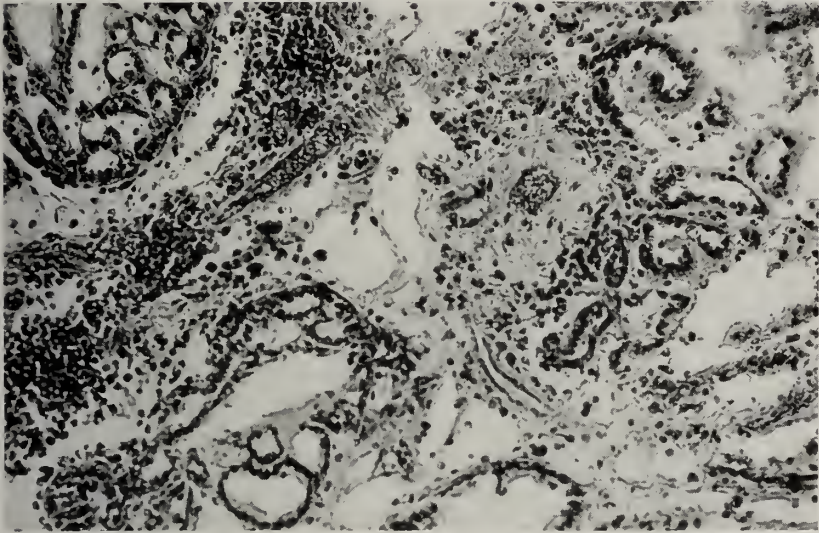


FIG. 209. Lymphangioma of the cheek which has undergone reaction. The cysts are empty causing the endothelium to appear cuboidal. Some of the septa are infiltrated with round cells. Areas where the vessels are small and the perivascular connective tissue abundant may resemble glands.

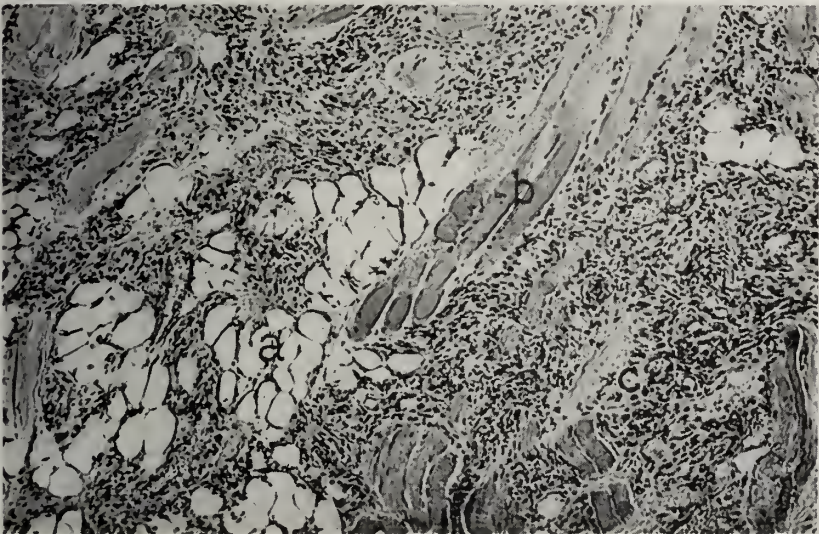


FIG. 210. Lymphangioma of the tongue which has recently undergone reaction: *a*, lymph spaces; *b*, muscle fibres of the tongue; *c*, round celled infiltration and new formed connective tissue. It is the increase of this connective tissue and the formation of lymph cysts which causes the enlargement after reaction.

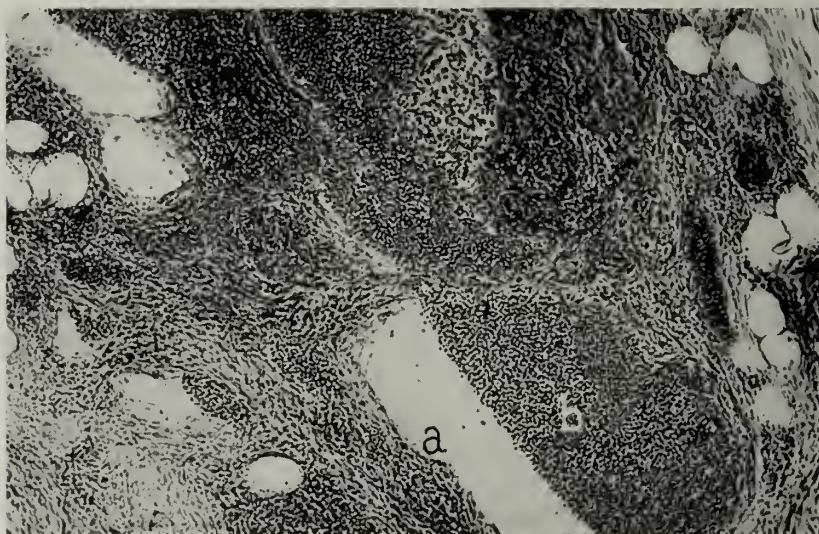


FIG. 211. Lymphangioma of the buttocks. The tumors formed a thick mass. It was made up largely of connective tissue and lymph follicles: *a*, lymph cyst partially filled by, *b*, lymphoid tissue. Because of the dominating lymph nodules such tumors are really lymphomas.

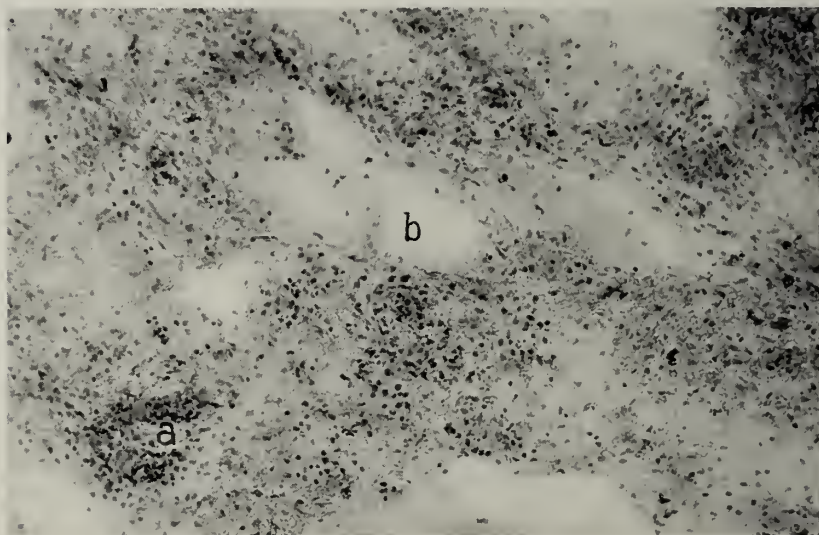


FIG. 212. Cystic lymphangioma in a state of acute reaction. The picture is that of edema of the septa: *a*, area of round cell infiltration; *b*, cyst narrowed by edema of its walls. The edema is so great as to almost completely obliterate the smaller lymph channels. The round celled infiltration is most pronounced about the blood vessels.

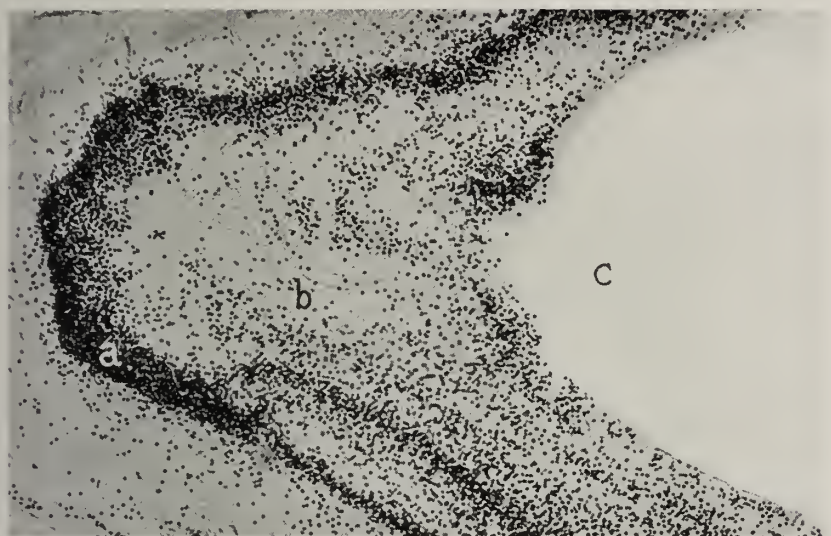


FIG. 213. Cystic lymphangioma in a state of acute reaction; *a*, collection of lymph cells on the cyst wall; *b*, coagulated lymph containing lymph cells in the meshes; *c*, fluid lymph. The coagulated lymph is granular and widely separates the connective tissue fibres. The cells are very deeply staining.

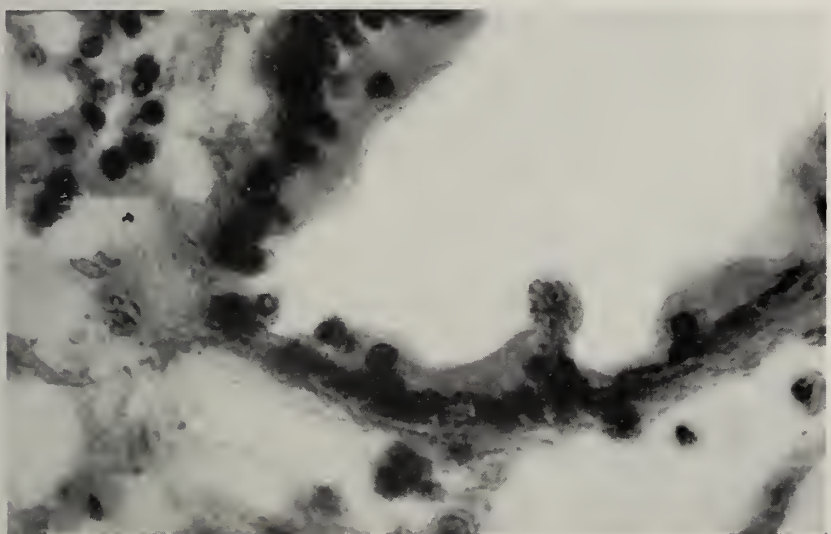


FIG. 214. Cystic lymphangioma in a state of reaction. The cyst is lined by high endothelium. To the left the connective tissue is edematous and contains lymph cells. The high endothelium lining the vessel indicates that they are participating in the reaction. The round cells likewise are deeply staining.

siderable mass remains though the lymph escapes. If hardened before section the lymph is coagulated and the original size of the lymph spaces is manifest (Fig. 202). In this state the lymph cysts resemble the poly-



FIG. 215. Cavernous lymphangioma. F., age 4. Pendulous tumor of axilla, present since birth. Excision. Cured 9 years.

cystic lesions of the parenchymatous organs, kidney, liver, pancreas and spleen. This is particularly impressive when associated with lymph cysts of the peritoneum (see volume on pathology of the peritoneum).

When malignancy supervenes there is a progressive enlargement of the affected area, increase in the size of the subcutaneous blood vessels and a general fixation of the tumor mass to the surrounding tissue. The

whole mass becomes firm to the touch without evidence of inflammatory reaction.

Histology. In uncomplicated cystic lymphangiomas the architecture, as in the simple form, is not impressive; merely cystic spaces in the connective tissue lined by a flat endothelium which lies on the thin con-



FIG. 216. Cross-section of a cavernous lymphangioma. Numerous cavities more or less separated by septa are apparent.

nective tissue septa (Fig. 208). In some cases the endothelium is high, giving the slide a glandular appearance (Fig. 209). Or the septa may contain a large number of undifferentiated cells, probably embryonal. These may be so numerous as to suggest malignancy to the inexperienced pathologist (Fig. 209), the lymph spaces may extend into the surrounding fatty tissue or between the muscle fibres, displacing and destroying them (Fig. 210). In these situations more or less well formed lymph follicles

may lie between the lymph spaces or may project into their lumen (Fig. 211).

When the tissue is in a state of reaction the cellular picture is that of any acute infection (Fig. 212). The cell infiltration is made up of round cells, polynuclears being conspicuous by their absence. It seems therefore to be a lymphatic reaction rather than a true infection. Coagulated lymph may partly occlude a lymph cyst (Fig. 213). The difference is notable when the skin is broken by accident or design. In such cases the polynuclears are abundant due to secondary infection.

The picture is sometimes confused by the shape of the lining cells. When the lymph spaces are empty their walls contract and the endothelium appears cuboid or even columnar (Fig. 214). Septa may appear as papillary projections into the tumor suggesting glandular proliferation, especially when the tumors are cut across before fixation.

No apology is needed for a detailed presentation of the histology of the lymphomas in reaction because some grievous errors have been made in the laboratory by even experienced pathologists. It is easier to interpret these tumors at the operating table than in the laboratory.

Cavernous Lymphangiomas. This type comprises the huge tumors made up of large individual or multiple cysts. These have been termed "hygromas," meaning moist tumors. Whoever named them this evidently cut into one during the process of removal. They are most commonly located about the neck, clavicular and axillary regions, less often in the sacral region. In this situation they may resemble atypical meningoceles and may be continuous with intrapelvic tumors. They may be entirely retroperitoneal producing huge tumors.

Pathogenesis. These tumors are usually obvious at birth. They form large baggy, often pendulous masses (Fig. 215). They may remain unchanged for many years. They are less prone than the cystic type to reactive changes and consequently to intermittent enlargement. When in a state of reaction they may simulate a cellulitis and are sometimes cut into. This reaction is sometimes initiated by the injudicious application of X-rays with the idea of obliterating the cystic spaces.

Pathology. The cystic mass is soft but not compressible for while connection with the surrounding lymphatics has been demonstrated, this may be ignored in the clinic. The overlying skin is normal in color and is unchanged except in those cases which are associated with simple lymphangiomas of the skin. Not uncommonly there may be tumors in several regions which may intercommunicate, the most common combination being the supraclavicular with an axillary tumor. In such cases one tumor may be compressible at the expense of the other. If the second

tumor be not recognized a false notion of compressibility of the tumor under examination may be entertained and the tumor confused with a blood cyst.

When cut into the cysts collapse and the surgeon has but little to show the anxious mother but when removed intact and hardened before sectioning the form of the spaces is apparent (Fig. 216). The more deeply lying tumors may be so complicated by interdigitations that the removal of the tumor intact is a technical impossibility.

Histology. The microscopic picture does not differ from the preceding form. When in a state of reaction edema rather than cellular infiltration makes up the mass of the tumor. The reason probably is that the tumor is located in loose cellular tissue devoid of an abundant blood supply. Even the connective tissue in the septa is loose and contains but few blood vessels. Lymphoid tissue is less abundant than in the cystic type; though those situated in the submaxillary region may contain lymph follicles perhaps native to the neck and not an integral part of the tumor.

ELEPHANTIASIS

This condition consists in a proliferation of the skin and subcutaneous tissue producing an enormous thickening of the affected part, generally a leg, less often of the genitalia and rarely of an arm or a part of the face and very rarely the breasts. The endemic form observed in some countries, notably Brazil, Egypt and India which is due to the *Filaria sanguinis hominis*, need not concern us here. The type observed here is due to a variety of special causes which produce disturbances in the vascular and lymphatic systems.

The essential factors are hindrance to the lymph flow generally associated with some irritative condition resulting in occlusion of the lymphatics. Even those beginning as diseases of the veins likely have as the chief exciting factor the occlusion of the lymphatics incident to the periphlebitis. Therefore the division into two general types is more or less arbitrary.

1. The Lymphatic Type. The chief characteristic of this form is huge enlargement of the affected part brought about by increase in the subcutaneous tissue.

Pathogenesis. Acute inflammation such as recurrent attacks of erysipelas or prolonged cellulitis from injury may initiate the process. The acute exacerbations of lymphangitis are often mistaken for attacks of erysipelas. I have seen an acute lymphangitis produce a temperature of 105° F. with edema of the entire limb. Save for the presence of the skin reaction of erysipelas the courses of the two diseases are similar. The lymphangitis, like erysipelas, tends to subside in a week or ten days. In

lymphangitis however, the entire area is involved spontaneously; the course is not progressive as is erysipelas. These inflammations apparently result in the obliteration of the lymphatics as well as stimulation to growth of the connective tissue. These are particularly pronounced if the lymphatic glands are destroyed by the infective process or removed by the surgeon. This type is prone to follow bubos. Formerly when



FIG. 217. Elephantiasis of the calf. F., age 42. Gradual enlargement for 12 years. Never any acute trouble. Numerous small lymph cysts within the skin about an ulcer which began three weeks ago.

radical excision of lymph glands in this condition was practiced the occurrence was not infrequent. After such an operation I once saw the external genitalia in a male attain truly equine proportions.

Pathology. The one impressive thing is the size of the affected part (Fig. 217). It is firm to the touch, does not pit on pressure and is but little affected by pressure. The skin is pale and tense. Within the skin small thick-walled vesicles can be made out in many but not in all cases.

Histology. Loosely arranged connective tissue bundles, inclosing few small cells with large deeply staining nuclei and an abundant structureless mucoid material filling in between the fibre bundles comprise the microscopic picture. It resembles much the histology of fibroma molluscum.

2. The Venous Type. More common than the lymphatic type, and usually less developed, is that group associated with varicosities of the veins which have undergone repeated inflammations. To what degree these are due to the venous congestion and to what degree there is an associated though secondary occlusion of the lymph vessels is not easy to say.

Pathogenesis. The most common cause of this type is obliteration of the deep veins through thrombosis as after labor or surgical operations, or from inflammation with thrombosis of varicose veins either with or without complicating ulcers of the skin. It is not easy to distinguish the two types for in the lymphatic form dilated vessels may appear in the skin and ulcers may appear secondarily. Usually the venous forms are relatively small. The rarer and usually less pronounced forms following burns, scarring from injuries probably act chiefly by affecting the veins but the lymphatics likely suffer to a certain degree.

There is much confusion in the literature from the failure to distinguish between elephantiasis and neurofibromas and fibroma molluscum which are tumor formations and do not result from lymph disturbance.

Pathology. The affected part is thickened, usually less whitish and glistening than the lymphatic form. The skin may be reddish or purplish in color. The appearance suggests edema though it pits on pressure but little or not at all, but may be bluish. In long standing cases the skin may be much thickened by an eczematoïd condition with or without exudation. In fully developed cases the affected part is tense elastic and does not pit on pressure. The skin is elevated in folds, most marked above the ankle or there may be wart-like protuberances. The tremendous masses seen in the endemic form do not develop in the type here discussed.

When cut into the tissue is white, sometimes pearly white, myxomatoid in appearance. In older forms the fibrous tissue is more pronounced so that parallel bundles can be made out in the thickened tissue. In more recent cases there may be an exudation of clear lymph-like fluid on the cut surface.

In long standing cases the mucoid-like material may extend through the muscles. On the other hand, the muscles may be converted through a process of myositis into a keloid-like tissue which creaks under the knife.

The lymph channels may be enormously thickened so that they are easily visible and distinctly palpable—in one of my cases larger than a slate pencil.

Histology. The slide shows a general thickening of the connective tissue of the skin as well as the subcutaneous tissue. The typical picture is made up of a meshwork of interlacing fibres in the interstices of which are many ovoid cells with well stained nuclei and pale protoplasm. The fibre bundles are separated by an abundant myxoma-like substance staining but faintly. In the long standing cases, particularly those which have resulted from acute infections the proportion of fibrous tissue may be greater, even to the formation of keloid-like fibrous strands. Likewise in the neighborhood of thrombosed veins or near ulcers, when they exist, there may show a more abundant connective tissue. In general the development of fibrous tissue is more pronounced than in the lymphatic type. This is particularly true of the skin and subcutaneous tissue.

Literature

Hemangiomas. Blood vessel tumors of the skin play not a small part in the literature. They are so diverse and so many different opinions have been held that a somewhat lengthy quotation from the literature seems warranted. Ribbert (*Geschwülstlehre*, Cohen, Bonn, 1904, s. 164) in harmony with his general views on the unicentric origin of tumors includes the blood vessels. Even he admits that they are congenital in origin and that when the tumors increase in size it is due to the widening and lengthening of the vessels and to the proliferation of the connective tissue. In rare instances dilated vessels not previously apparent appear in later years as in a case reported by Hildebrand (*Deutsche Ztschr. f. Chir.*, 1890, xxx, 91) in which the first tumor appeared on the thumb and later like lesions appeared on the forearm and shoulder. These various lesions were separate congenital anomalies.

Much confusion has been caused in the misinterpretation of malignant tumors developing in the site of a previously existing angioma. In such cases it is the pre-existing maldeveloped cells associated with the vessel lesions. In the nevi-angiomas melanotic tumors may arise and in the keratoid angiomas epithelial tumors develop.

Perhaps it must be admitted that newly formed vessels may play the leading rôle in the formation of tumors. They must be rare for even distinguished pathologists, when they write books, use borrowed cuts. The surgeon may dismiss them as non-existent. When very vascular tumors are formed one may be certain that it is the associated tissues that are doing the mischief and that the tumor is very malignant. However, granulation tissue has been mistaken for tumor and wholly needless operations performed.

The tumors derived from blood vessel endothelium, the peri- and endo-vascular endotheliomas belong to a different category. Even these are losing caste. Many tumors previously accepted as of such origin are now known to be of epithelial origin and when the developmental anlagen are more carefully considered their stock is likely to undergo further depreciation.

Warren (*Surgical Observation on Tumors*, 1837) referred to a class of tumors which he terms "erectile tumours." The nevi materni he described as a congenital aneurism by anastomosis stating that "although they have a disposition to grow to a certain extent they rarely become widely spread," and described spontaneous cure by ulceration

or loss of vitality. He mentioned their threatening aspect and described a case degenerating into cancer. Tumors made up of larger blood spaces he described as "accidental aneurism by anastomosis" and "congenital tumors of the veins." Pulsating vessel tumors he considered either congenital or traumatic in origin.

Coats (*A Manual of Pathology*, 1883) described vascular tumors or angiomas as plexiform or capillary angiomas and cavernous tumor or lymphangiomas. The capillary type he described as almost always of congenital origin.

Senn (*The Pathology and Surgical Treatment of Tumors*, 1900) condemned the term "cirroid aneurism" or "aneurism by anastomosis" pointing out that all plexiform blood vessel tumors are true tumors. He described the embryonic misplacement of angioblasts as the histogenesis of angioma and stated that all capillary angioma are congenital; cavernous angioma may be of traumatic origin. Lymphangioma were described as of the same histological elements as hemangioma but of more delicate structure and the vessels filled with lymph.

Campbell (*Venous angioma of skin showing beginning malignancy*, *Jour. A. M. A.*, 1907, 48, 2000) reported several cases of venous angioma of the skin and expressed the belief that venous angiomas do not take on malignant characteristics but the epithelium overlying may develop carcinoma. Borrmann's (*Ziegler's Beitr. z. path. Anat.*, 1907, 40, 372) case (cited by Ewing) of hemangioma of the breast developed metastases from which the patient died. The original tumor had the histological appearance of a benign angioma; the metastases appeared more cellular but were clearly angioma.

Ribbert (*Virchow's Arch.*, 1898, 151, 381) in writing of angiomas described the injection of the afferent vessels of angiomas with the solution returning through the efferent vessels, yet no solution was found in the vessels of the normal tissue surrounding and lying next to tumor vessels, thus showing the independence of the angioma circulation. Ewing (*Neoplastic Diseases*, Ed. 3, Saunders, Co., 1928, p. 243) takes Ribbert's findings as an argument that angiomas are distinctly neoplastic and the process arises in an isolated segment of a vessel congenitally predisposed to autonomous growth.

Bell and Inglis (*Brit. Jour. Surg.*, 1926, 13, 696) give an excellent description of a vascular tumor developing following trauma along the area supplied by the posterior tibial artery. Dissection of the amputated limb failed to show a posterior tibial artery present and this the authors interpret as the developmental defect leaving angioblastic tissue separated from the vascular system and becoming active following stimulation by trauma. Livingston and Klemperer (*Arch. of Path. and Lab. Med.*, 1926, 1, 899) describe a case of an angioma developing following prolonged exposure of the chin to X-ray. The tumor reappeared repeatedly after excision. Pulford and Adson (*Surg., Gynec. and Obst.*, 1926, 42, 846) describe a case of benign fibroangioma of the scalp associated with epithelioma of the overlying skin. Jaffe (*Arch. Path.*, 1929, 7, 44) explains that hemangioma may be simple cavernous proliferation of flat endothelium-lined vessels with little or no stroma or a more complicated type of either cellular or embryological syncytial stroma from which vessels differentiate in a variable relative quantity and either type may prove malignant. He says it is impossible to determine microscopically whether or not angiomata are benign but believes that metastases of angioma with mature stroma is doubtful. There are many transitional stages between pure angiomata and vascular sarcoma. A case is described of multiple angiomata of skin and internal organs which the author believes are of simultaneous and independent origin.

Acton (*Jour. Med. Res.*, 1927, 15, 355) points out that the term "saroid" is a misnomer and many of the tumors so described are in reality hemangioma. He describes a series of cases which he believes developed in the skin following irritation caused by toxins and bacteria circulating in the blood. Gray (*J. Path. and Bact.*, 1929, 32, 337) describes an autopsy case of a large infiltrating vascular tumor of the liver which he believes to be a malignant hemangiomatous endothelioma originating from Kupffer's cells; no metastases were found. Winslow (*Arch. of Surg.*, 1929, 19, 829) reports a case of hemangioma of the scrotum and cites nine other cases in the literature.

New and Clark (*Ann. Otol., Rhin. and Larung.*, 1919, 28, 1025) report 3 cases of progressive angioma of the larynx. Johnson (*Jour. A. M. A.*, 1928, 90, 1108) writes of a case of hemangioma of the forearm with several calcified areas showing in roentgenograms and Dunn (*Ann. of Surg.*, 1925, 82, 880) points out the tendency of thrombi in angioma to calcify lends an aid in diagnosis of deep-seated angioma by X-ray. Putschar (*Ztschr. f. Kreislaufforsch.*, 1929, 21, 495) gives a general account of angioma of the vertebrae and points out the frequency with which inconsequential ones are found at autopsy. Makrycostos (*Arch. f. klin. Chir.*, 1929, 155, 663) gives a similar account and points out that if symptoms are caused at all they are usually seen in young individuals.

Connell and Hay (*Canad. Med. Jour.*, 1930, 22, 75) describe a case of a woman, aged 31, who died from cord compression at the sixth and seventh thoracic vertebrae caused by hemangioma. Lyle (*Ann. Surg.*, 1929, 89, 633) describes the ball valve action of a phlebolith changing the size of a hemangioma of the chest wall with various attitudes of the patient. Davidoff (*Am. J. Path.*, 1929, 5, 141) had a hemangioblastoma of the cerebellum. He refers to several such cases reported by Lindau. Lindau's cases had such tumors in other organs.

Cushing and Bailey (*Tumors Arising from Blood Vessels of the Brain*, Chas. Thomas Pub., 1928) in an excellent monograph on blood vessel tumors of the brain divide such tumors into two classes: angiomatous malformations and angioblastomas. The authors believe the first group are probably not neoplastic but are congenital malformations in the vascular system. They may be telangiectatic, venous or arterial. These more commonly occur in the cerebral hemisphere. The angioblastomas the authors described as true tumors composed of angioblastic elements having a congenital anlage. They nearly always occur in the cerebellum and are occasionally associated with cystic formations and angiomatous tumors in the retina and spinal cord, cystic kidney, cyst of the pancreas and liver as described by Lindau. The authors think many tumors previously described as gliomas or meningiomas belong to this last group.

Lymphangiomas. Senn (*Pathology and Surgical Treatment of Tumors*, Saunders, 1900, ed. 2, p. 465) defined lymphangioma as "a tumor composed of lymphatic vessels produced from a matrix of angioblasts." Classifying them as capillary, cavernous and cystic, he believes the first type to be always congenital whereas the cavernous and cystic types may develop anytime after birth. Cystic lymphangioma are described as the result of dilatation or confluence of lymphatics of the tumor and possessing the greater tendency to growth. Neither type tends to destroy life. Bland-Sutton (*Tumors, Innocent and Malignant*, Hoeber, 1922, ed. 7) found lymphangioma of the same groups as described by Senn but believed cystic lymphangioma, which he described as occurring about the neck, axilla, and thoracic wall and adjacent parts, as congenital. Adami (*Principles of Pathology*, Lea and Febiger, 1910) divides lymphatic growths into lymphangiectasis (simple, cavernous and cystic) and lymphangioma proper. He believes under the first group should be placed the cystic hygroma, macroglossia and the slightly protuberant skin areas in which many lymph capillaries are found. Tumors classed as "lymphangioma proper" are only those showing a notable proliferation of lymphatic endothelium. This may appear in simple lymphangiectasis in the young. Ewing (*Ibid.*) writes concerning lymphangioma: "In the pathogenesis of these conditions many factors are concerned and it is thus more difficult to distinguish between lymphangioma and lymphangiectasis than between true and spurious hemangioma. . . In the origin of lymphangioma it must be assumed that there exists predisposition resulting from an embryonic disturbance similar to that assumed for hemangioma. Of the nature of this disturbance nothing definite is known but the congenital origin of most lymphangioma is a striking feature in their etiology." Stillman (*Jour. A. M. A.*, 1911, 57, 756) reported two cases of lymphangiomatous cysts of the omentum and gives a thorough review up to 1911, with summary of the 19 cases other than his in the literature up to that time. All were not considered lymphangioma cysts by the original reporters but from description of the cases Stillman believes they were of lymphatic origin. Grausman

and Jaffe (*Ann. Surg.*, 1928, 87, 66) report a similar case of a lymphangioma cyst occurring in the greater omentum. From a study of the tissue the authors conclude such tumors are true blastomas arising from undifferentiated mesenchyme. Cysts are formed by obstruction to either new formed or pre-existing lymphatics but the latter never enter into the neoplastic growth. Another similar case is that of Fisher (*Ann. Surg.*, 1928, 87, 872) occurring in a child 4 years old. Mehlinger (*Beitr. z. path. Anat.*, 1927, 78, 434; *ab. Cancer Rev.*, 1928, 3, 175) gives a macroscopical and microscopical description of a lymphangioma of the interventricular septum of the heart with death from partial coronary occlusion. He states only two previous cases have been reported. Lloyd (*Bull. Johns Hopkins Hosp.*, 1929, 44, 149) has since reported a similar case affecting the arterioventricular node with death due to partial heart block. Franklin and Cordes (*Jour. A. M. A.*, 1924, 83, 1741) reports a case of lymphangioma occurring in the orbit, causing exophthalmos, which was successfully removed. In a review of the literature he states only 13 such cases have been reported. He maintains the view that such tumors are lymphangiectasis and not true lymphatic neoplasms. Gallagher (*Surg. Clin. N. Am.*, 1928, 8, 625) reports a case of lymphangio-endothelioma occurring in the region of the parotid duct, and Moorehead (*Ibid.*, 1929, 9, 329) a case of the same type of tumor in the upper lip of a child.

CHAPTER IX

Diseases of Blood and Lymph Vessels

HAVING considered in the previous chapter the tumefactions which the vessels produce, a consideration of the diseases to which they are subject is next in order. We have seen that diseases complicate the tumefactions. The diseases are even more intimately associated with the results of diseases which must be considered separately, no matter how artificially, in the subsequent chapter, thrombosis and embolism.

A really scientific classification of the diseases of the blood and lymph vessels would lead to needless perplexity to the surgeon. The simplest classification must recognize the three main divisions: the veins, arteries and lymphatics. The following outline may serve for the basis of the discussion:

- I. Diseases of the Veins
 - A. Dilatation—the Varicosities
 - B. Phlebitis
 - a. Acute Phlebitis
 - 1. Noninfective
 - 2. Infective
 - b. Chronic Phlebitis
 - Nutritive
 - Pus Microbe Infection
 - Tubercular
 - Syphilitic
- II. Diseases of the Arteries
 - Dilatation Aneurysms
 - Endarteritis
 - Gangrene
 - Arteritis Nodosa—Buerger's Disease
 - Arteriosclerosis
- III. Diseases of the Lymphatics
 - Acute Pus Microbe Lymphangitis
 - Sporotrichotic Lymphangitis
 - Tularemia
 - Chronic Lymphangitis

DISEASES OF THE VEINS

In harmony with the outline just proposed the surgical lesions of the veins may be divided into the: 1, varicosities; 2, the reactionary which may be due to infection or to non-infection, the phlebitis—usually nutritive disturbances; 3, the thrombotic, generally the result of one or both of the preceding must be considered as an end product of either of them or both associated. The consideration of thrombosis as a separate chapter is artificial but its close relationship with its associated lesion, embolism, makes such consideration necessary.

In the following account I shall endeavor to present only those conditions that have been more or less securely established by clinical experience. Even by such limitation one must needs be brief for the literature is vast and confusing and the clinical material abundant.

Varicosities. Venectasias these are, walls standing away from each other, literally as the word means, resulting in widened lumens, making for greater carrying capacity which they do not do, and there is the rub. They become the white-collar gentry in the circulation, capacity without speed—they become impediments to the normal function, and as it should be, they suffer the most from their own dereliction.

Pathogenesis. Dilatation of veins may be the result of inherent weakness of the walls of the veins and perhaps equal weakness of the surrounding soft parts. Long standing, which deprives the vessels of the intermittent propelling force of muscular contraction, plays a part in some cases. Perhaps the emphasis the Germans place on this by citing the frequent occurrence of varicosities in baker apprentices unwittingly gives a clue. A young man who adopts the baker's trade, spending his days kneading bread and fashioning cookies, must possess weaknesses not confined to his legs. At any rate the static type in the young in this country is rare but does occur (Fig 218). These may remain merely as dilatations for many years. Sooner or later the stasis results in malnutrition of their walls and secondary disturbances result.

Varicosities of the scrotum, close rival to the legs, present much the same problems. There are more varicoceles in Sunday-school than on the baseball diamond. To explain this is a delicate and precarious procedure. What is cause and what is effect is not always easy to determine. It is the path of least resistance for the boy to have his ears polished and go to Sunday-school rather than to bolt the back fence and make for the sand lots. Thus some lads may make virtue of a weakness, and, it may be said in passing, the lack of weakness may make virtue easier and point to the fundamentals of treatment.

The lack of exercise favors phlebectasias. Therefore dilated veins in early years indicates a constitutional weakness often hereditary and one's vision must encompass more than just the dilated veins before instituting treatment. The patient, rather than the veins, may require treatment.



FIG. 218. Juvenile varicose veins. M., age 31. Has had dilated veins since he was 16 years old. Mild pain when much on feet.

The dame of numerous progeny presents a somewhat different problem. She learns to stand for a lot, and it is not all figuratively speaking either. The iliac veins seldom free from pressure by fetal head return their blood against great resistance. The toil entailed in excessive

domestic labor leading to prolonged standing, is only partly relieved by the muscular exercise made necessary by the intermittent pursuit, over wood and dell, of that same cranium that short years before had retarded the venous return. These experiences, repeated more times than the modern flapper can count, leads ultimately to the dilatation of the veins of the lower extremities. These dilated veins are anatomic states rather than diseases. They differ from the adolescent varicosities in that the cause is pressure added to the normal column leading to the dilatation, while in the static the normal column is sufficient to cause a dilatation. In the former the cause can be removed, in the latter it is inherent.

But one other region requires mention as a common site of dilated veins, the pampiniform plexus. The commonest cause is the prolonged dilatation required to remove sewage from the coming generation associated with compression by the fetal parts which prevent the escape of the blood to the larger veins. This is the one common cause. Whether esthetic contemplation is a cause or result of pampiniform dilatation in the varicosities in the male evidence available does not indicate. The fact that both disappear in the course of time removes this form of venectasia from the realm of surgical concern.

In themselves dilated veins produce no symptoms. The recognition of this fact is worthy of emphasis. To attack veins merely because they are large is without result as any surgeon knows who has unwittingly removed varicose veins of the scrotum and thereby attached for life to his clientele a sexual neurasthenic.

Just where the border-line between simple phlebectasia and phlebitis lies is sometimes difficult to determine. As a matter of clinical convenience it is well to put those cases which make trouble in the latter category, though it must be admitted that simple dilatation may lead to edema of the legs, but this edema brings with it sooner or later changes in the walls of the veins. Furthermore such a division helps to exclude other causes of swelling not due to local disease, such as the puffy legs of the neurasthenic, the incipient myxedema and the like.

Pathology. To understand the dilated veins they must be studied in the living. Those observed incidentally only are typical. When the patient comes because of her varicosities there are secondary changes which call the patient's attention to them. Uncomplicated varicosities are seen as wide channels with thin walls. The wide channels make it at once evident that the valves are inadequate to prevent stagnation. In fact valves may be difficult to find after the veins are removed and split open. Perhaps they have been obliterated by the distention of the walls of the veins. Unable to perform their function they have turned politician and

have joined the bootleggers of illicit blood. When removed from the body they contract and the walls appear actually thicker than a normal vein merely because the wide expanse of wall when reduced to smaller dimensions makes a thicker tube (Fig. 219). The wall is glistening and homogeneous indicating an excessive development of fibrous tissue.



FIG. 219. Varicose veins of leg removed intact. M., age 18. The coiling of the vessels is well marked in the upper part of the picture.

Irregular sacculations here and there are noted. They are unattached to the skin unless previous inflammation has caused them to adhere.

Histology. The intima is unchanged though the contraction of the vessel wall may cause it to appear thickened. In very long standing cases the media may show nothing of muscle fibres (Fig. 220). These may appear as wide channels even after removal.

Phlebitis. Inflammation of the veins may be divided into two groups, the noninfective and the infective. This classification is satisfactory only

from a clinical point of view. The noninfective is so regarded when an obvious source of infection is not present and the infective when it is an obvious extension from a pre-existing infection.

Noninfective Phlebitis. The term "inflammation" is applied rather loosely to these affections for in many, perhaps in most, there is no actual inflammatory change present. No apologies are needed for the use of the term in this connection for it is common practice in pathology to apply the term to any process that is not understood. The common cause of

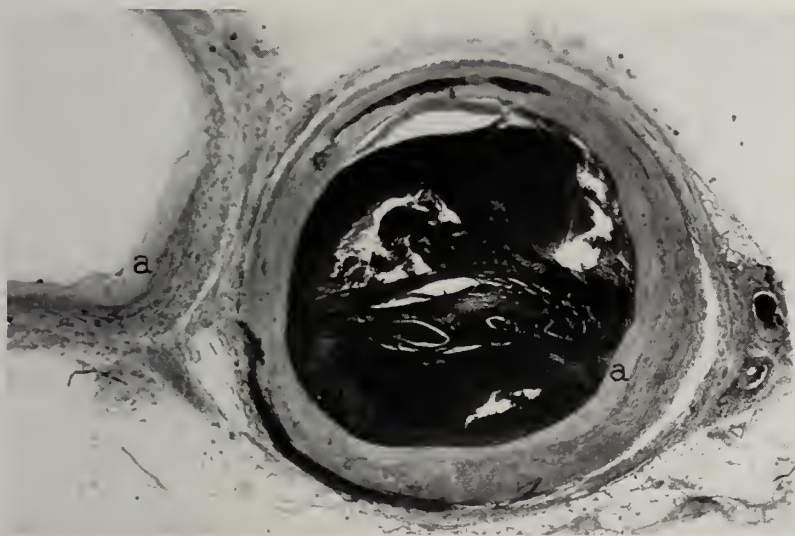


FIG. 220. Varicose vein which before removal was widely dilated. The walls are thick, involving chiefly the subintimal layer, *a*, and the adventitia which largely replaces the media.

irritation is a nutritive disturbance of the vessel wall. This irritation may be sufficient to produce a periphlebitis, or even a more or less complete thrombus in the vein.

Pathogenesis. The common site of phlebitis is the leg, generally in veins previously dilated. Sometimes there is a gradual thickening of the vessel walls producing a palpable tender cord without changes in the surrounding connective tissue or with simple hyperemia of the skin (Fig. 221). The nature of this process which induces coagulation is not clearly understood. Likely it is due to a disturbance of the vessel wall due to the unfavorable circulatory conditions. So long as the intima is intact thrombosis does not take place. Soon after thrombosis begins there is a definite reaction about the vein and in surrounding tissue from the irritation of

the clot. The reaction may end here and the organization of the clot results in a permanent occlusion of the vein. Upon the artificial induction of this process the injection treatment depends. In both cases new channels may be formed in the process of organization and the circulatory channel is restored.



FIG. 221. Thrombophlebitis. M., age 52. A week ago leg began to swell and was tender to touch. The vein is palpable as a fibrous cord.

The perivascular reaction may be so intense that the overlying skin is destroyed (*A. Fig. 222*) and the familiar ulcer of the skin with destruction of the vessel wall results (*B. Fig. 222*). Bumping of the leg, the site of varicosities, frequently leads to injury of the vein with thrombosis and extensive periphlebitis with ulceration of the skin and even of the vein and severe, even fatal hemorrhage, may follow. Actual suppuration about the vein occurs only when there is superficial infection from without.

When the skin is destroyed as just indicated secondary infection is of course inevitable and the result may be a true infectious thrombophlebitis.

Added to the purely static injury or even independent of it a trauma may cause reaction within the vein. This form is encountered in the most variable situations. The most common is over the tibia the result of a direct blow. Practically the most important, is injury to the popliteal vein leading to gangrene of the foot and leg and of the median vein



FIG. 222. Ulcer formation due to thrombosis of the veins. *A.* M., age 36. Dilated veins for 11 years. Since 2 weeks ago the leg has been swollen. Whole vein is palpable. At the upper border of the popliteal space the skin is becoming necrotic. *B.* F., age 42. Has had moderately dilated veins for many years. Recently an area as large as a dollar became inflamed which has resulted in an ulcer.

following phlebotomy or the injection of therapeutic substance (Fig. 223). Occlusion of the vein extends to adjacent and deeper veins leading to serious involvement of the extremity. Injury to the uterine veins during labor may lead to extension to the pampiniform and even the iliac and femoral veins producing the familiar milk leg. Even the lowly hemorrhoids, due to compression from the sphincter or direct injury, may become so altered that a phlebitis with thrombosis results.

A dividing line between the traumatic and infectious forms is difficult to establish. Infection may play a secondary part or may be the primary factor. In endophlebitis following labor it is often impossible to distin-

guish between the two forms. If the reaction subsides after a few days pure trauma may be assumed but if extensive cellular inflammation, possibly with abscess formation, we are certain that infection is present, whether primary or secondary it may be difficult to say.

Inflammation of the veins without clotting is possible when the irritation begins in the perivascular tissue. This condition is characterized by a thickening of the vein wall recognizable by palpation together with



FIG. 223. Thrombosis following injection of salvarsan. M., age 36. Evidently the operator missed the vein. Perivascular inflammation and thrombosis resulted.

spontaneous pain or tenderness on pressure. Long tender cords may be so produced. In most cases clotting at some point occurs. In such cases the clots are apt to be but loosely attached. Because the irritation approaches the intima from without this form of clot is but loosely attached to the vein wall and is most apt to be loosened and form an embolus. This observation is inserted here in passing. Its wider significance will be discussed in the chapter on thrombosis and embolism.

Pathology. Once coagulation within the vein occurs reaction in the adjacent tissue follows producing reddening of the skin with subcutaneous edema of a hard exudative type without there being definite cellular

infiltration (Fig. 224). Long continued this reaction may be productive and permanent thickening result. Tunneling of the clot may take place and the circulation be reëstablished or the collateral vessels may assume the burden and the circulation is restored.

A general thickening of the vessel due to infiltration of the wall itself, to the presence of a clot within the vein, but particularly to the reaction of the surrounding soft parts, makes the nature of the process at once apparent. More deeply lying veins may find expression only in the sur-



FIG. 224. Thrombosis within varicose veins. There is as yet no phlebitis and the surrounding tissue is not invaded by cellular infiltration. (Same patient as FIG. 221.)

rounding edema as is seen in the familiar milk leg following deep thrombosis. When cut across the deep red plug in the vein is at once apparent (Fig. 224). The reddening of the skin over the vein and the infiltration of the surrounding soft parts make the nature of the process obvious. The thrombotic hemorrhoids furnish convenient objects for study in this type. An exudate may form between the clot and the vessel wall manifesting a loose connection between the two. This is conveniently observed in the readiness with which the clot is turned out in the ubiquitous cutaneous hemorrhoids. The contemptible little objects have within them pathological processes of vast clinical import.

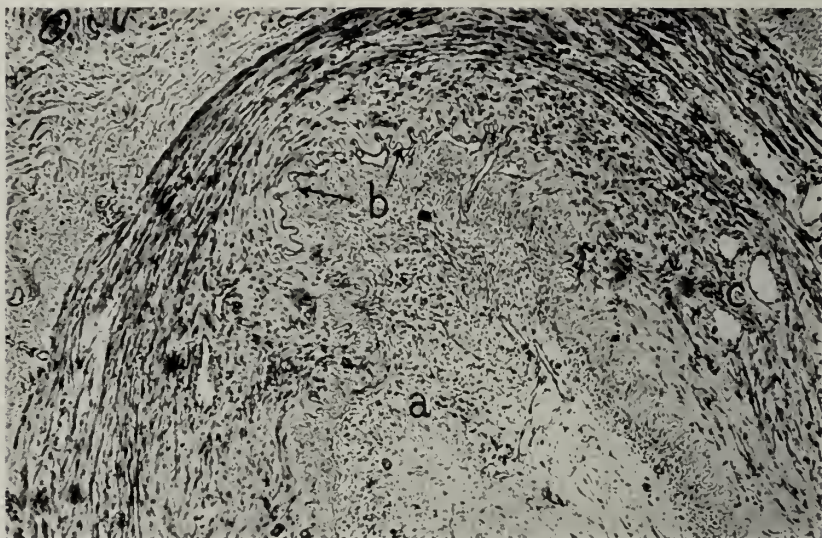


FIG. 225. Completely organized clot: *a*, clot; *b*, endothelium of vessel preserved; *c*, dilated vaso vasorum. In such cases nothing remains but a fibrous cord. This state is most often observed in deep thrombosis, following aseptic trauma or at some distance from the focus of infection.

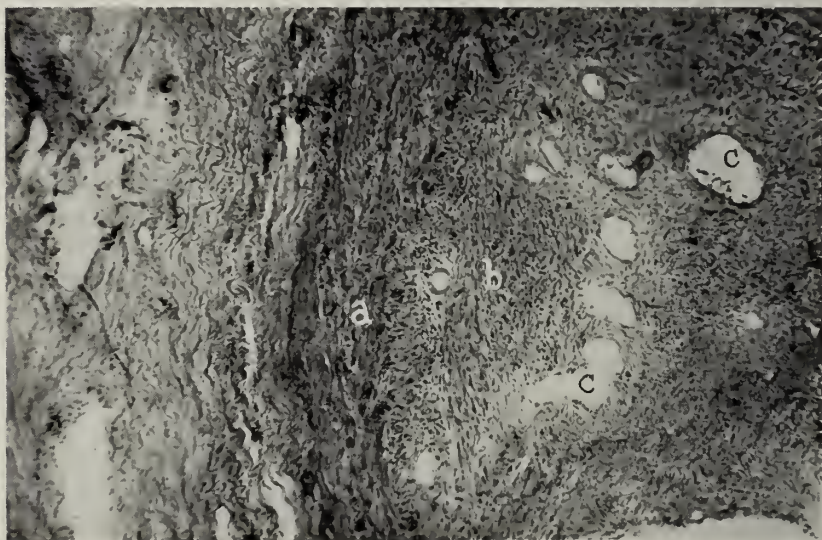


FIG. 226. Organized thrombus in a case of noninfective phlebitis; *a*, vessel wall; *b*, newly organized clots; *c*, newly formed vessels. In such cases the restoration is but partial but may result in the cure of the disease. This is the form most commonly seen in thrombosis of superficial veins.

Histology. The early changes in phlebitis are to be seen in the intima. The endothelial cells become high, even columnar. The vessel walls undergo varying degrees of reaction even to necrosis of the overlying skin. This subject has been dealt with in the chapter on ulcer (Figs. 235 and 236). Organization of blood clots in the noninfective cases usually results in complete occlusion (Fig. 225). If the coagulum so produced is fibrinous in character connective tissue promptly forms a permanent union with the vessel wall and the lumen is occluded. This may be attended by the formation of new vessels within the clot (Fig. 226).

Infective Phlebitis (Septic Thrombophlebitis). This type is the result of direct extension of an infective process from the adjacent tissue into the veins or from injury of the intima from an infection situated elsewhere in the body. The extension of a septic process from the cavity of the uterus into the pampiniform veins is perhaps the most classic, and those secondary to adjacent infections as seen in appendicitis, is the most common example. It differs from the non-infective phlebitis chiefly in that bacterial colonies are associated with the clot.

Pathogenesis. In the case of the involvement of the pampiniform plexus, infection is conveyed to the vein directly from an infected area, the invading bacteria themselves producing the injury to the intima. Sometimes an infective process adjacent to the vessels approaches its walls and injures the intima which produces a coagulum. A periphlebitis and then a phlebitis precedes the injury to the intima as is commonly seen in appendicitis. Here the primary point of departure of the infection is from the mucosa. The primary infection may be minimal and travel by the way of the capillaries to the veins as is seen in the common sinus thrombosis following infection of hair follicles about the lip. Direct extension through the vessel wall is seen in lateral sinus thrombosis in mastoid disease.

Because of the bacterial toxins within the vein a granular thrombus is produced and this being incapable of forming fibres directly is prone to become detached and forms an embolus. This process may follow reactive conditions independent of actual bacterial invasion as in the cystic vein in nonsuppurative cholangitis.

Actual pus may form within or about the vessel wall or within or about the clot. This may result in an extensive cellulitis with abscess formation. A clot which is infected in one part may not be in another. For instance a thrombophlebitis in the pelvis may find extension down the femoral vein which at some distance from the point of infection may be sterile. Obviously there is no dividing line between the infected and the noninfected phlebitis.

The great majority of thrombophlebitides ultimately do become organized and either become rechanneled or permanently occlude the vein. The infected clots are more apt than the noninfected to become channeled by new vessels. The commonest example is the formation of clots in the veins of the pampiniform plexus with extension of the process into the femoral vein causing the so-called milk leg which results in the permanent occlusion of the femoral veins while the pampiniform veins recover. Like conditions follow many infectious diseases, notably typhoid fever. The injury to the vessel wall likely resulting from direct contact of the circulation bacteria but other factors active in the production of a thrombus may be present.

As a result of perivascular inflammation the lymphatics may become involved. The result is interference with the function of the lymphatics and a general thickening of the parts results. In the lower extremity this finds expression in the familiar milk leg. It is this process rather than the occlusion of the deep veins that produces the permanent thickening of the subcutaneous connective tissue producing a mild form of elephantiasis. The vein occlusion plays its most important part when the patient becomes ambulant. The familiar skin ulcers complicate the picture when stasis from posture is added to the injured tissue.

Pathology. My pathology days encompassed the time when surgeons did hysterectomies for post-puerperal pelvic thromboses thus providing for the pathologist excellent material for study of infected thrombi though the procedure was somewhat severe for the patient, for the most of them later came to autopsy. In such cases the veins were filled with solid red clots which were loosely attached to the vessel wall or even separated from it by a more or less cloudy exudate. In such cases it is only the lack of a propelling force that prevented a detachment of the clot from its mooring.

Following the formation of the clot, in the case that the patient survives, a phlebitis and a periphlebitis develops and a serous and cellular exudate forms about the vessels to such a degree that a palpable mass forms in the pelvis, high up when slight or low down if extensive, producing the parametritis of the older writers.

Varicosities of the extremities furnish a less fulminant object for study. When cut across the hard indurated mass produced by the thrombosed vessels associated with cellular infiltration of the adjacent tissue shows the vessels distended with clot. The perivascular tissue may be pale even translucent from the abundant exudate in the tissues.

Histology. The cell structure varies greatly. In mild cases there may be extensive infiltration of round and polynuclear cells about the vessels

but in severe infections there may be an absence of cells and the endothelium be replaced by a coagulated mass warranting the use of the term "diphtheritic" applied by some investigators.

The interesting feature in this type of vein inflammation is that the organization is equivalent to the healing of a wound by second intention. The vessels within the wall of the vein dilate and take an active part in the organization of the clot (Fig. 227).

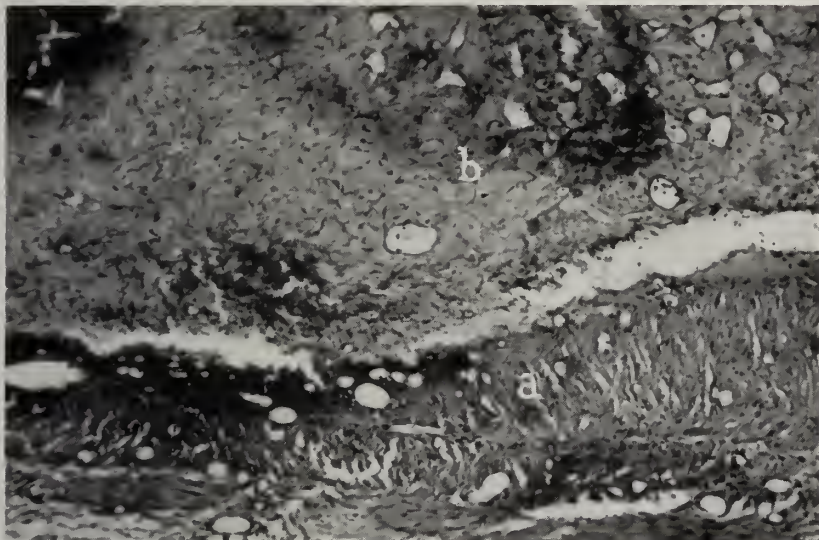


FIG. 227. Organization of a clot: *a*, vessel wall; *b*, organizing clot with newly formed vessels. These vessels within recently organized clots ultimately become narrowed and the vascular occlusion is complete.

Chronic Phlebitis. Inflammatory reaction may take place due to static or infectious causes. The veins in varicosities may become thickened as the result of repeated subacute reactions.

Syphilis and tuberculosis, and less commonly actinomycosis may involve the walls of veins.

DISEASES OF THE ARTERIES

The purpose of the arteries is to convey blood to distant parts of the body. Naturally the chief diseases to which they are subject have to deal with the interference with this function brought about by the narrowing of their lumen. Aside from the disasters due to the transportation of clots from a distance this occlusion is due to the narrowing of the lumen resulting from the thickening of the vessel walls. The final

results are death of the tissues through failure of adequate blood supply. The failure of circulation may be gradual, due to the narrowing of the lumen alone, or it may be complicated by a secondary thrombosis, or by some constitutional condition which makes the nutrition supplied inadequate whereas it would be sufficient to nourish a normal tissue.

Therefore it becomes necessary to divide the disorders of the arteries into three classes. The gradual narrowing of the vessel wall incident to old age is often uncomplicated and may properly be classed as *senile*.



FIG. 228. Senile gangrene. M., age 76. Since 8 months second toe gradually became dry and hard. Recently first and fifth toes are becoming black and the top of the foot is swelling. Since then intense pain. Died of pulmonary embolism.

Even here thrombosis may complicate the process. The nutritional disturbances complicating lessened blood supply is limited chiefly to diabetics so the end process is properly called diabetic gangrene. Differing from these is the vascular affection characterized by occurrence in early adult life appearing often as recurrent acute exacerbations involving the veins as well as the arteries. Thrombo-angiitis obliterans seems the ideal name for this group for that is just what happens.

In all of these it is the end product that concerns the surgeon—the

gangrene. Since each requires different management they must needs be discussed separately.

Senile Gangrene (Arteriosclerosis). Though the changes in the vessels in this disease are associated with advancing years the calendar cannot be depended on to distinguish this type from the others because constitutional diseases and particularly heredity modify the influence of time.

Pathogenesis. As a result of the gradual thickening of the vessel wall the parts affected become blanched in appearance and cold to the



FIG. 229. Senile gangrene. M., age 78. Foot cold for many months. First noted black spot above ankle. Toes and soles involved during past few weeks. Thigh amputation.

touch. Soon the skin becomes inelastic, then gradually changes to a deep black color (Fig. 228). A toe usually shows the first changes. Sometimes the first changes are noted at some other part of the extremity, commonly at the outer border of the foot, less commonly above the ankle (Fig. 229). Usually higher and higher areas are reached until increasing pain compels amputation. In very slowly developing cases a line between the gangrenous and viable tissue forms and spontaneous amputation takes place (Fig. 230).

The affected part is blanched, responds slowly from anemia produced

by pressure. Increased sensibility and associated coldness may be the forerunners of gangrene. On the other hand increased redness and increased sensibility are even more ominous. From either beginning the skin becomes increasingly dry, gradually becoming more dark in color until complete mummification is reached.

Here as usual pain is the cry of dying tissue. So long as there is gradual mummification pain is not produced. When dying tissue becomes



FIG. 230. Senile gangrene, spontaneous amputation. M., age 70. During past two or more years gradual necrosis of toes of right foot with spontaneous amputation. Left foot began several months ago. Complete mummification of the toes. Line of demarcation distinct.

opposed to viable tissue a reaction takes place and pain attends. When a line of demarcation forms the pain ceases. In those cases in which a thrombus hastens the closure of a vessel the pain may be as violent as that which follows an embolism.

As in many vascular diseases contractions of the vessel walls seem able to produce intermittent exacerbations of the disturbance expressed as attacks of acute pain and disturbed function, the familiar intermittent claudication. This is the result, it is supposed, of temporary increased limitation of the blood supply the result of spasmodic contraction of the

vessel wall. Exposure to cold may precipitate such attacks. Nervous excitation likewise seems to act in the same way. In one of my patients the attacks seemed to be brought on by the anticipation of going for his morning drink, making it impossible to do just that which he most desired.



FIG. 231. Senile gangrene of second toe. M., age 72. Had corn removed, followed by gangrene which extended to ankle.

Though once definite tissue damage has begun the process may occupy months or even years. Commonly the disease gradually extending from toe to foot and often the calf. When the process extends thus slowly it is due to gradual changes in the vessel wall. When the changes in the vessel walls are complicated by a thrombus the extension of the gangrene is much more rapid. This is attended by severe pain which

causes the patient to seek radical relief. It is this reaction of the soft parts that warns the surgeon of a complication which demands amputation higher up than the apparent involvement. The point of chief occlusion of a vessel and the point where the complicative thrombosis is to be sought is the point where the vessel arises from the larger trunk vessel. This should be the guide in the selection of the point of amputation and not the apparent extent of the gangrene. In the case of the foot this point is at the division of the popliteal artery. This is the reason that it is but seldom that amputation below the knee is effective. Even though the thrombus may extend well up the femoral vessel the collateral

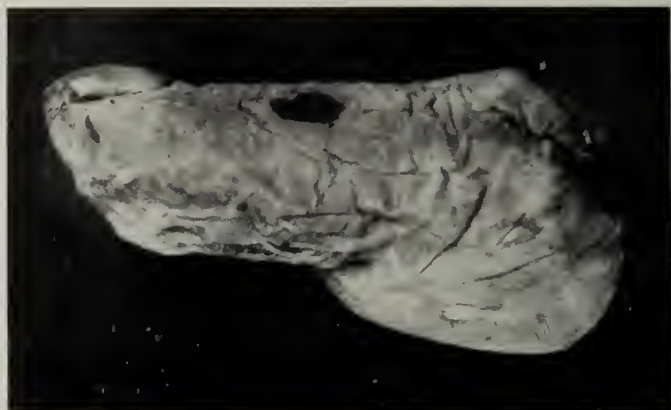


FIG. 232. Early senile gangrene. M., age 70. Left leg amputated three years ago for gangrene. Three weeks ago right great toe became cold and numb; the skin cold, dry and shriveled. Gangrenous spot on top. Amputated through calf; reamputated through thigh three weeks later.

circulation is usually such that it is possible to amputate at the point of election, the lower thigh.

One fact must always be remembered by the surgeon: a blood vessel capable of supplying adequate nutriment under normal conditions may not be able to bear an additional strain. Even small operations, such as the removal of corns, may be the starting point of a senile gangrene (Fig. 231). Apparently the discomfort of impending gangrene causes the luckless patient to search for causes of his trouble and the minor disturbances, before unnoticed, are pointed out to the surgeon as the source of his trouble. Likewise slight trauma or exposure may initiate the process and lead some innocent person into a damage suit.

Pathology. The mummified parts are dry and hard as though hardened in formalin (Fig. 232). This may terminate more or less gradually



FIG. 233. Arteriosclerosis in senile gangrene; *a*, thickened media; *b*, intima but little involved; *c*, partial thrombus partly organized.



FIG. 234. Diabetic gangrene. F., age 62. Some disturbance in great toe for ten years. Since two years it has been ulcerated and discharged a bloody flow. Was amputated six weeks ago. Failed to heal and right great toe became black. Healed with insulin.

in the adjacent more or less normal tissue but sometimes the line of demarcation may be sharp (Fig. 231). It was the formation of this line which the older surgeons awaited before operating. Mummified areas when cut into are very hard, even impossible to cut. In the early acute exacerbation the soft parts are edematous, even hemorrhagic depending on the degree of destruction of tissue. Often the involvement of the skin extends to a higher point than the deeper parts. This is most likely to be true in the uncomplicated cases. In those accompanied by thrombosis the opposite is true.



FIG. 235. Diabetic gangrene. F., age 64. Great toe began to turn black 4 months ago. Spread to foot in past two weeks. But little pain. Amputation.

The vessel walls are thickened appearing as pinkish or pearly glistening rings. Commonly clots are found in the lumen often at a distance from the site of gangrene. It is quite common to find the femoral artery to be occluded by a clot at the point of amputation in the lower thigh. The vessel walls present definite thickening, sometimes calcification so that ligation becomes an uncertain procedure.

Histology. Hyalinization of the vessel wall; the destruction of the elastic fibres and in some cases the deposition of calcareous material in the vessel walls are present. The thickening involves chiefly the media, the intima being but little or not at all involved. When it does become affected associated thrombosis begins. This may be partial or complete (Fig. 233). When calcareous processes reach and involve the intima thrombosis does not take place.

Diabetic Gangrene. Vascular changes, in the main like those in the aged, occur in the diabetic at a much earlier age. That the resulting death of tissue is nutritional rather than mechanical is proved by the fact that under the influence of modern treatment beginning gangrene is halted and the destruction already wrought recovers.

Pathogenesis. The initial process is usually a reddening of the skin, then ulceration accompanied often by pain. In the aged diabetic there may be a mummification, a senile gangrene in a diabetic. Even here the



FIG. 236. Diabetic gangrene of the foot. General thickening of the walls of all the vessels. Partial occlusion with associated clot at *a* and *b*. There is everywhere marked perivascular thickening of the connective tissue.

diabetes modifies the process (Fig. 234). In general the diabetic gangrenes are more hyperemic than the senile. The lesions may remain local for long periods, even years. When there is complete vascular occlusion, usually instituted by accessory thrombosis, the process is more rapid. Usually the affected parts become mottled or completely gangrenous (Fig. 235) and may dry or slough depending on the rapidity of onset and the degree of vascular occlusion. Because of the rapid progress conservative amputations are even more luckless here than in the senile form. Fortunately, as already noted, the treatment of the diabetes by modern methods may result in the recovery of the gangrenous process.

Pathology. Ulceration rather than mummification represents the typical lesion (Fig. 234). The affected parts are hyperemic, the subcutaneous

tissues moist and they may be hemorrhagic. The vessels show thickening which may be but little apparent to the naked eye. Extensive thrombosis is usually the most striking finding in the laboratory in specimens which reach the amputation stage. Fortunately now the necessity for amputation seems almost a thing of the past.



FIG. 237. Moist gangrene. M., age 78. Ten days after having wandered away for two days, walking about in mud, gangrene to mid-calf. Cured by lower thigh amputation.

Histology. The microscopic findings are not unlike those in the arteriosclerosis which attends senile gangrene (Fig. 236). Usually the degenerative changes are less pronounced and aside from those incident to thrombosis but little may be noted.

Moist Gangrene. As a corollary to the two preceding types of gangrene that type, in which destruction of tissue is too rapid to admit of mummification of the affected part, may be mentioned.

Pathogenesis. Sudden occlusion of a vessel from any cause may lead to rapid death of tissue. Embolism produces the most typical examples. Minor injuries or exposures may excite thrombosis in those predisposed through senile or other changes. The line of demarcation between the sufficiently and the insufficiently nourished is established after a time if the patient survives. The period need not be awaited for the site of the trouble can be determined by examination.



FIG. 238. Obliterating thrombo-angiitis. M., age 27. Since 2 years cramps in calf of left leg. Had red spot on foot, doctors lanced it. Had periarticular sympathectomy elsewhere. Pain worse since. Skin swollen and ulcerated. Amputation. Now pain in right thumb 4 weeks; swollen, tense for 2 days, blanched except for tip which is black.

One of the common causes of moist gangrene is injury to the vein leading to its occlusion. The most common cause is injury to the popliteal vein or of the short saphenous at the point of entrance into the popliteal. The occlusion of the femoral vein is less commonly the cause. Injuries involving these veins should be the signal for a cautious prognosis. A cold foot following injury to one of these veins is a distressing discovery.

Pathology. The affected part is moist, cold, deep red, bluish or bluish black. The epidermis is commonly loosened and slips under the examining hand (Fig. 237). When cut into the soft parts are soggy with edema.

Histology. The microscopic evidence is dependent on the causative lesion, injury or chronic vascular disease and then always the determining thrombus.

Thrombo-Angiitis Obliterans (Buerger's Disease). This disease is characterized by a more or less general involvement of the blood vessels but chiefly affecting the arteries of the extremities, resulting in a thrombosis of the vessels which frequently terminates in gangrene.

Writers generally emphasize the common occurrence of this affection in the Jewish race. All of my cases have been in Gentiles. I am disposed to conclude that the disease is most commonly observed in those races of which the practitioner sees the most. The only reason I see for



FIG. 239. Obliterating thrombo-angiitis. M., age 58. Pain in feet for 18 years. Aspirin and codeine at intervals for past 5 years. Toes first became blanched and painful, then red, then black and fell off. When the toes become black pain ceases. No treatment.

attempting to make a racial disease of it is the quite common involvement of the hands.

Pathogenesis. The beginning of the disease in many cases is signalized by intermittent claudication, an intermittent limping caused by cramplike pains in the calf, often associated with a numbness. This intermittent character of its manifestations suggests that vascular spasm plays a part early in the disease. In this it differs from vascular changes which cause both senile and diabetic gangrene. It differs also in that it affects chiefly young persons.

After weeks, months, or even years of the intermittent symptoms just noted more permanent lesions appear. The affected part becomes pain-

ful, even excruciatingly so. With this is a blanching (Fig. 238) or a blush of the surface, a condition augmented when the limb is allowed to hang down, and disappears when the limb is elevated. Though the skin is reddened in the beginning, it may become pearly white.

Following this, as a result of injury or without, necrotic areas appear. This is preceded usually by a peculiar tense edema which may or may not present a mottled or generally reddened skin. Usually the process



FIG. 240. Bone changes in a case of obliterating thrombo-angiitis. M., age 58.

begins as small necrotic patches at the end of the toes, frequently about the nails. Gangrene may begin before the disappearance of pulsation in the dorsalis pedis and posterior tibial arteries. The necrosis extends to the foot and may involve the leg. It is usually the increasing pain over weeks and months that impels to amputation rather than the advancing gangrene.

In slowly developing cases there may be spontaneous separation of the affected parts (Fig. 239) but the truce is only temporary. The disease invariably extends after a time demanding ultimate amputation.

The general nature of the affection is evident from the not infrequent association with a noninfective phlebitis. The veins may be found to be occluded being represented by a fibrous cord but usually there is asso-

ciated tenderness and edema of the surrounding parts. Successive areas may become thus involved. These vein changes may precede the appearance of evidence of arterial involvement, may be associated with it or appear only after the deeper lesions have become well established.

While the legs are the site of this disease in the majority of cases the arms are by no means immune. The occurrence in this locality is particularly noteworthy because of the disposition to mistake it for primary nerve lesions.

Pathology. The general nature of the pathological process is suggested by the name first proposed by von Winiwarter, namely endarteritis

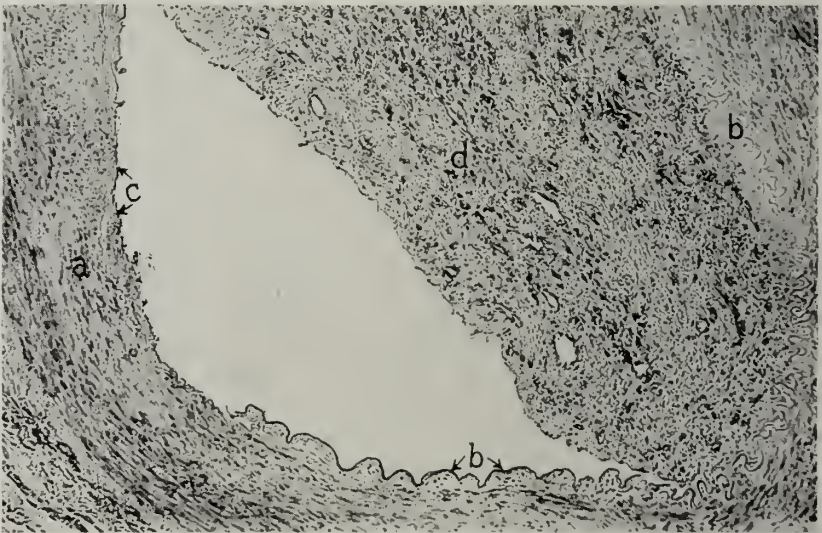


FIG. 241. Artery in thrombo-angiitis obliterans; *a*, wall of the artery but little thickened but infiltrated with round cells; *b, b*, the basement membrane retained; *c*, the basement membrane lost; *d*, organizing clot.

obliterans. In fact at the work-bench this seems a more appropriate name than that proposed by Buerger which heads this chapter which undisputedly best describes the clinical picture.

The soft parts about the vessel are usually edematous and the smaller vessels turgescient. Thrombosed or completely obliterated veins may be encountered. The arteries are thick walled and filled for the most part with a yellowish or reddish coagulum. There is a question whether this is the essential lesion. At the proximal point of the lesion one encounters a fibrotic area which appears to be the initial lesion, the product of the disease of the vessel wall, and the extensive clot filling the vessel may be

but the tail of the clot, hence the accidental though essential terminal lesion.

The bone changes have been but little described but there is a rarefaction and atrophy in the bones which may appear early in the course of the disease and is pronounced in cases of spontaneous amputation (Fig. 240).

The necrosis gradually shades into the normal without the formation



FIG. 242. Aneurysm of popliteal artery. M., age 72. Senile gangrene. Aneurysm discovered during amputation for gangrene.

of a sharply dividing line though in the early stages there may be a more or less definite border suggesting an ulceration rather than a necrosis.

Histology. The typical lesion is a fibrotic plug more or less obliterating the lumen of the vessel. This plug often shows a tunneling by newly formed vessels, indicating nature's attempt to restore its lumen. How this is brought about is the question. I can abundantly confirm von Manteuffel's observation that endothelial desquamation is common, a condition not observed in any other lesion. It would be wholly in con-

formity with general pathological processes to look on this lesion as the initial process which gives rise to the formation of a thrombus which ultimately leads to occlusion of the lumen of the vessels and serving as the starting point for the formation of the long vessel-filling clot which is so prominent in the gross specimen after amputation (Fig. 241).

What gives rise to the initial lesion is a question. That it is general is evidenced by the fact that the veins may be involved preceding, in association with, or following the arterial lesion, as already mentioned. There

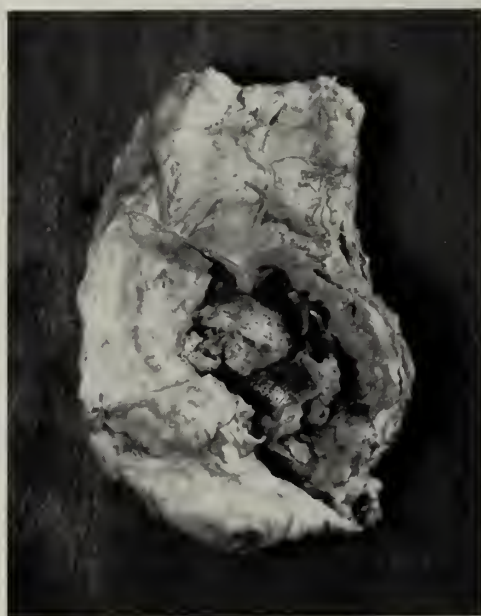


FIG. 243. Popliteal aneurysm completely occluding the artery, leading to gangrene of the foot.

are periarterial fibroses as well as changes in the vessel walls. These consist in a generalized thrombosis and in many cases an increase of elastic fibres. All this would lead one to search for the initial cause in the walls of the vessels and to regard the thrombus formation only as the terminal and in a sense an accidental factor.

The minute changes consist of fibrotic changes while the acuter lesions show round cells, even polynuclear leucocytes. These might be secondary to the formation of the clot and really a result of the terminal clot formation. However the fact that the round cell infiltration is found where there is no clot speaks against this assumption. In superficial veins it

seems something happens to the intima and a thrombus forms at this point. This may precede the arterial involvement. Following this a reaction occurs in the walls of the vein with the usual cellular activities. The terminal stage may be permanent occlusion of the veins or the re-establishment of the circulation.



FIG. 244. Traumatic aneurysm. M., age 21. Fell through window. Blood spurted from wound; pressure applied, whole inside of thigh was swollen. This disappeared in a few weeks and a pulsating lump remained. Large cavity medial to femoral artery and connected with it. *Insert*, M., age 13. Shot himself with .22 revolver. Aneurysm of circumflex artery. Removed.

Buerger's disease seems to be essentially a reactive process whereas the changes underlying the senile and diabetic gangrene are degenerative.

Aneurysms. Aneurysms, as the word indicates, are permanent widenings in the lumens of vessels. True aneurysms are of two types; the spontaneous, those due to disease of the vessel walls; and the traumatic, which are preceded by traumas which injure one or more coats of the vessel resulting in so weakening the wall that a dilatation follows.

Spontaneous Aneurysms. The majority of this type occur in the aorta as a result of syphilitic arteritis and concern the internist and the pathologist though the surgeon must know of their existence. Those due to nonsyphilitic arterial changes are found in the larger peripheral vessels.

Pathogenesis. In rare instances aneurysms of the aorta erode the sternum producing pulsatile tumors protruding above the sternum or from erosion of vertebrae may simulate cord affections.

It is chiefly those which involve the peripheral vessels which concern the practicing surgeon. The most common site is the popliteal artery



FIG. 245. False aneurysm of popliteal artery. M., age 32. Injured by gunshot wound. Large inflammatory mass covered by hyperemic skin. Sent to clinic as abscess. Cured by ligation.

(Fig. 242), next the femoral, but may appear anywhere. They produce ovoid or more elongated tumors, situated in the line of the vessel and usually more or less pulsatile in character. Sometimes the sacculations become filled with blood clot occluding the vessel curing the disease if a collateral circulation is established. Sometimes the clotting completely occludes the vessel producing gangrene. Sudden pain attends these accidents suggesting embolism.

The dilating sac may cause pressure pain or when clotting forms within them the surrounding tissue is irritated and a painful swelling is produced. The growing tumor usually produces pain which leads to its recognition.

It is important to recognize the fact that in this type of aneurysm the vessel dilates because the walls are diseased. It is necessary to recognize this since obliteration of a part of the cavity by suture leaving a canal for the passage of blood, has been advocated for the cure of the aneurysm. The remaining part may dilate again because at best the new course is

made of diseased tissue. My experience has been that these obliterative methods result in the occlusion of the entire vessel and while a cure is affected it comes about by producing a complete occlusion just as ligation of the vessel does. In both cases the integrity of the circulation in the distal parts is dependent on the collateral circulation.

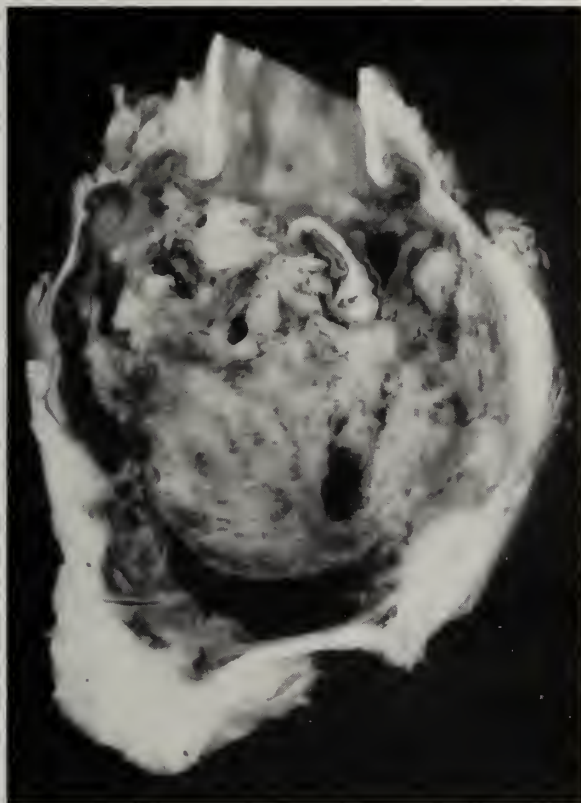


FIG. 246. Traumatic aneurysm of the femoral artery. M., age 67. The interior is occupied by an organizing clot. The wall at the left is formed by the thinned arterial wall and on the right largely of the adjacent soft parts.

Unlike aneurysms of the aorta those of the peripheral vessels seldom perforate spontaneously.

Pathology. The tissues about aneurysms may be inflamed if the vessel dilates rapidly or forms more or less extensive clots within its lumen. Usually there is no perivascular involvement and the lesions may be palpated as a fusiform mass often slightly tender to the touch and distinctly pulsatile. After removal or when opened on the operating table

the sac is filled more or less with blood clot but in rarer instances the wall of the sac is more or less smooth perhaps showing grossly the sclerosis which underlies the dilatation. Sometimes as noted the entire cavity may be filled with a coagulum (Fig. 243).

Histology. The contained clot may show some degree of organization but more commonly the structure is that of a coagulum. The vessel wall shows the usual changes of arteriosclerosis. Plaques may be formed in the intima but usually the changes consist of hyalization of the media with replacement of the muscle fibres.

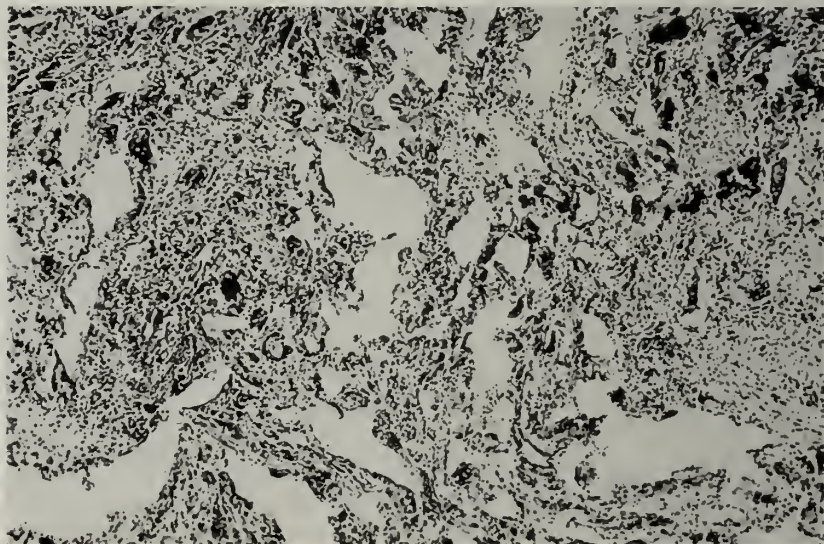


FIG. 247. Organizing clot from a traumatic aneurysm. The newly formed fibrous tissue is interspersed by wide blood sinuses.

Traumatic Aneurysms. As this term indicates these follow injury to the vessel wall. This is by far the most common type which confronts the surgeon.

Pathogenesis. Usually in civil practice a stab or a gunshot wound which destroys one or more coats of the vessel, permitting a dilatation of the weakened area is the cause. The result is the dilatation of one part of the wall. The dilatation of this type irritates the surrounding tissue less than the spontaneous variety. In this type discovery of a pulsatile tumor at the site of the injury first calls attention to its existence. The blood enters freely into the sacculation producing a distinct pulsation. The disturbance it causes is usually the result of pressure on the surround-

ing tissue. They usually attain a certain size and remain so. The protrusion is usually obvious to inspection and the site at once makes their origin obvious. (Fig. 244). In the stage of formation the surrounding tissues are so agitated that a more or less diffuse inflammation may be present so that the true nature of the disease may be masked (Fig. 245). This mistake has led to incision.



FIG. 248. Cirroid aneurysm of the facial artery. F., age 29. For 15 years a gradually developing tumor over the right cheek. Soft, compressible, pulsating. Ligation of the facial artery produced only temporary improvement.

Pathology. These, more commonly than the spontaneous type, are formed by smooth walled sacs. There is seldom spontaneous clotting because the vessel wall aside from the site of injury is normal. Clotting may form which goes on to organization (Fig. 246) thus producing a partial occlusion of the sac.

Histology. The microscopic changes are those of defect rather than pathological changes in the vessel wall. The dilated area may be formed by a pseudo-sac contributed to by the surrounding tissue. The organizing clot may be extensively vascularized giving the appearance of an angioma (Fig. 247).

Unusual Lesions of the Vessel Walls. A number of lesions of the vessel walls are sometimes included under aneurysms.

Spurious Aneurysm. The chief of these is the so-called spurious aneurysms. These are due to extravascular accumulations of blood resulting from the injury of all the coats of the vessel wall. If the opening heals the clot absorbs. If it does not heal the constant addition to the extravasated blood causes irritation to the adjacent tissue which reacts by forming a fibrous wall about the clot. In long standing cases the fibrous capsule may be so complete that a differentiation between these and the traumatic aneurysms just described cannot be made.

Arterio-Venous Aneurysm. When an adjacent artery and vein are simultaneously injured healing may result in a communication between the vein and artery. The result is that the blood may escape from the artery into the vein resulting in the disturbance in the peripheral circulation.

Aneurysmal Varix. This consists of a dilatation and lengthening of a peripheral artery, usually the temporal, radial or ulnar. There results a much elongated vessel producing a more or less pulsatile tumor (Fig. 248).

DISEASES OF THE LYMPH VESSELS

In the performance of their function as sewers of the system lymph vessels now and then are called on to transport substances, chiefly bacterial, which prove harmful to their walls. There results then an inflammation, usually acute, rarely chronic. These may be divided into the pus microbe or bacterial lymphangitis, the sporotrichotic and the tularemic. The simple chronic may follow any low grade infection. The diagnosis of tubercular lymphangitis was a common one before the above named specific lesions were understood.

Acute Pus Microbe Lymphangitis. Following superficial skin infections the lymph channels become inflamed and becoming perivascular the infection imparts a hyperemia of the skin which results in the formation of a red streak which leads from the site of infection to the lymph glands. Usually in the course of some days or weeks the inflammation subsides. Less commonly the local lymph glands suppurate and very rarely the infection becomes systemic resulting in grave forms of generalized infection.

Sporotrichotic Lymphangitis. Following infection by the *Sporothrix* inflammation extends along the course of the lymphatics which results in so thickening them that they are palpable beneath the skin. Very commonly at intervals localized abscesses form which break down forming

ulcers as large as the thumb nail or larger (for illustrations, see *Minor Surgery*, Hertzler and Chesky, Mosby, St. Louis, Ed. 2, Fig. 67).

Tularemia. In this condition the local ulceration is followed by a mild lymphangitis often not sufficient to produce a palpable cord. The first manifestation is usually a suppurating gland in the axilla (see Fig. 69, *ibid.*).

Chronic Lymphangitis. In this condition the lymph channel is palpable as a thickened cord feeling much like the vas deferens. The wall becomes fibrotic which may become permanent.

Literature

Diseases of the Veins. A very extensive summary on diseases of the veins is contained in Benda's recent book (Lubarsch-Henke, *Handb. d. spez. Path. Anat.*, Vol. II, pt. 2, p. 913). There is distressingly little in our own literature.

Thrombo-angiitis obliterans. Von Winiwarter (*Langenbeck's Arch.*, 1879, 23, 202) first suggested that it be called "endarteritis obliterans." Buerger's (*Am. Jour. Med. Sc.*, 1908, 136, 567) best describes the clinical picture (see also his monograph, "The Circulatory Disturbances of the Extremities," Saunders, 1924). Manteuffel (*Zentrbl. f. Chir.*, 1902, 3) observed that endothelial desquamation is common, a condition not observed in any other lesion. Recently two excellent papers have appeared; Silbert, Kornzweig, and Friedlander (*Arch. Int. Med.*, 1930, 45, 948) and by Barron and Lilenthal (*Arch. Surg.*, Oct. 1929, 19, 735). The former call attention to the fact that the condition may be generalized, the latter have studied the blood changes.

CHAPTER X

Thrombosis and Embolism

THROMBOSIS, as a process inseparably associated with diseases of the blood vessels, was considered in the preceding chapter. To the pathologist there is apparently no dividing line between thrombus formation and the embolism resulting therefrom. We are concerned here with that phase of thrombosis which is associated with embolus formation, and more particularly that which follows some surgical procedure. This relationship of embolism and operations is so generally recognized that a vast literature has been written on "post-operative embolism." To state the ugly truth even more plainly, post-operative embolism is that type caused by some act of the surgeon. Fortunately for the peace of mind of the surgeon, not all embolisms following operations are the result of his acts. Other conditions bring it about and its occurrence may take place independently or even in spite of his activities. Small salve, this, but it is sufficient to warrant a consideration of the broader aspects of the problem, otherwise we would scarcely need extend our inquiries beyond the simple problem of the reaction of vessel walls to injury.

Since there are so many factors involved in the formation of thrombi and their escape which the surgeon does not understand, a more extensive consideration is needed, for it is only by so doing that a broader conception of the process can be acquired. Even when an embolus finds its origin at the site of operation it is sometimes comforting to the surgeon to remember that there are, or at least may be, contributing factors that are beyond his control. Thrombus forming at the site of injury is easily enough understood, but thrombi form elsewhere where a vein lesion cannot be demonstrated or even hypothecated as, for example, in the femoral thrombi following noninfected operations on the appendix. The surgeon may with good conscience keep in mind the factors other than local disease and injury of the vessel walls underlying the process of thrombosis generally accepted by pathologists.

At the same time, it must be insisted on at the outset, the surgeon must hold fast to what he has seen in the local formation of thrombi in diseases and injuries of the vessels and not be led astray by the findings of the pathologists in the autopsy room. He has vastly more to lose than he has to gain by listening to them if he loosens for a moment his hold

on what experience has taught, namely that postoperative thrombi, directly or indirectly, are the result of his own acts. The failure to keep this in mind has led to institution, or commission of acts, such as stimulation of the circulation, changing the coagulability of the blood, which may further rather than prevent the tearing away of clots, necessary in the healing of vessels, and sending them on their missions of disaster.

Statistics are not necessary to remind the surgeon that thrombosis and its counterpart, embolism, are now the major problem in operative surgery. It causes more surgical deaths than any other preventable cause. Perhaps this statement may seem unnecessarily harsh to the surgeon but when postoperative embolism results from an elective operation he may well ponder what the result would have been had operation been avoided or postponed until such a time when the vessels he must needs ligate had recovered their normal state and made possible prompt and certain healing of the vessel wound. Important as the question is now it is apt to become much more so after we learn how many of the so-called postoperative pneumonias are really due to postoperative emboli. It is this responsibility that makes of the dreaded postoperative embolism, the untamed terror of all surgeons. Nothing remains more indelibly impressed on the mind of the surgeon than to see the results of his labor suddenly swept away by the lodgment of a blood clot in the lung or brain of his convalescent patient. The friends, joyous at the recovery of the patient, are thrown into consternation by the sudden disaster, and are so stupefied that the explanation that an escaped blood clot caused death seems a sojourn into the mystical and the surgeon cannot but have, in part, this feeling, so little does he know of the factors involved.

From the foregoing it is evident that we can profitably consider the problem of thrombosis and the resulting embolism under two headings, namely surgical and spontaneous.

Thrombus formation in its normal relation is a beneficent process, for without the formation of thrombi all operations would obviously be impossible. All our patients would bleed to death. Excessive or imperfect formation, on the other hand, seriously interfere with our plans. A normally forming thrombus is securely attached to the wall of the vessel at its point of origin but when there is some disturbance in the normal course or organization it is insecurely attached to the vessel wall and, escaping, it floats in the blood stream to lodge in some narrowing blood vessel and we have disturbance of function of that organ.

Because the subject of normal and abnormal thrombus formation is so broad in its physiology, its pathogenesis and clinical manifestations, it becomes necessary to examine all these phases somewhat in detail.

Though closely related to embolism it is necessary to consider thrombosis first as an entity. It is necessary first to understand the processes which form a normally organizing clot.

Definition. A thrombus is defined by Professor Welch as "A solid plug or mass formed in the living heart or vessels from constituents of the blood. Thrombosis is the act or process of formation of a thrombus or the condition characterized by its presence."

This is the definition of the pathologist. To attempt to distinguish between a clot and a thrombus may be regarded as a bold act. However, if the surgeon is to assume responsibility for postoperative emboli he should be allowed to define the limits of his responsibility. With this object in view it would seem warranted to regard the definition just quoted as applying to blood clots, being formed wholly from constituents of the blood. Thrombosis on the other hand is that phase of wound healing characterized by the precipitation of fibrin from the blood stream by the action of some element from the vessel wall which has for its purpose the permanent healing of the severed vessel or the repair of its injured wall. It is a process the product of elements from the blood stream plus elements supplied by the vessel wall. If this hypothesis is kept in mind the surgeon has a point of departure from which he can measure the degree of deviation of a given lesion from the primary purpose of nature. If the departure is the result of his own act he is in a position to consider whether a different course of procedure would have produced a different end result. Only knowledge of things that one can see or feel is of use to the surgeon. The concept here set forth at once aligns the process of thrombus formation with that of wound healing in general. The two processes are in fact identical. Knowing the factors which have to do with normal wound healing, as well as those conditions which disturb it, he can apply this knowledge unreservedly to the problem of thrombus formation.

Whether thrombus formation which result from general disease are to be regarded as clots or thrombi in the sense here set forth is another problem, for the changes produced by the disease may act in many ways besides affecting locally the walls of the blood vessels. Here he can do nothing but join hands with the internist and await the findings of the pathologist. Though he must plead ignorance, he has an alibi, the universal haven of derelicts.

Types of Thrombi. Two types of thrombi must be recognized by the surgeon. *First*, those due to injury of a vessel and, *second*, those, in so far at least as he is concerned, arising spontaneously.

SURGICAL THROMBOSIS

It seems desirable to consider thrombus formation under two headings as one does the healing of wounds, by first and second intention. In the case of wounds this is almost equivalent to a division of aseptic and infected wounds. Healing of thrombi by second intention is perhaps more complicated than the healing of other wounds, at least, one must admit as much out of respect for generally accepted opinion. The diversion is not great when one accepts a broader view of wound healing.

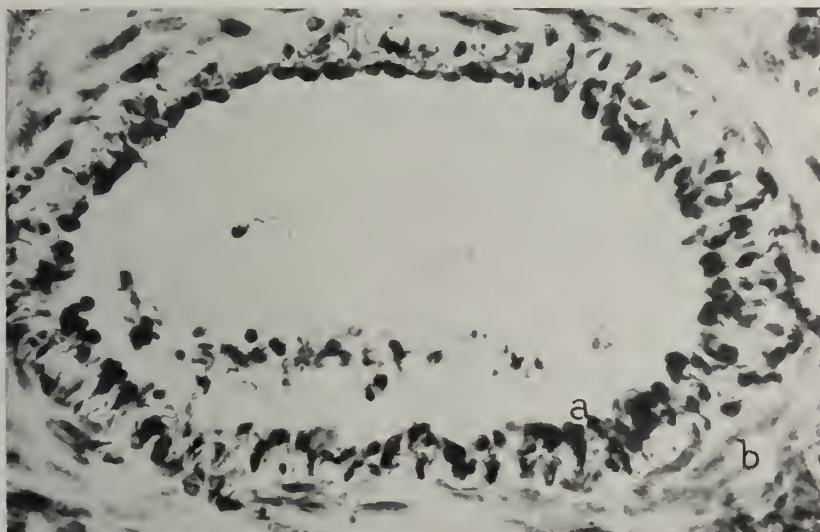


FIG. 249. Changes in the endothelium is the first step in the formation of a thrombus: *a*, endothelium much thickened; *b*, below the elastic membrane and cement substance is increased.

Failure of a wound to heal is as much influenced by general states as are thrombi but surgeons seldom bother to recognize them.

Thrombus Healing by First Intention. The initial factors in the formation of a thrombus in a normal vessel is the change in the endothelium of the blood vessel. It becomes higher, even columnar (*a*, Fig. 249) and the basement membrane becomes thickened (*b*, Fig. 249). This thickening of the subendothelial layer becomes very pronounced. This is particularly marked when the intima has been injured by a ligature (Fig. 250). The elevation of the intima has as a result the narrowing of the lumen, thereby lessening the space to be occluded by the organizing clot. This elevation of the intima is identical with the elevation of the serosa in

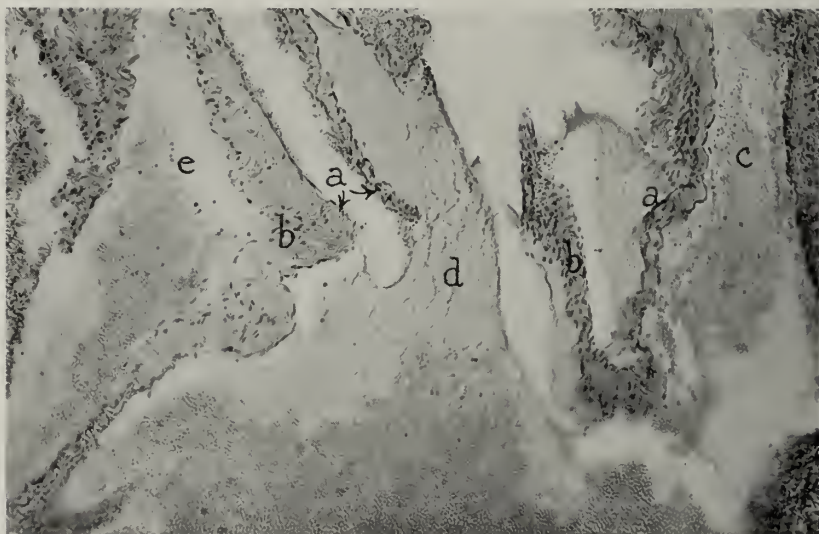


FIG. 250. The endothelial layer together with the basement membrane is elevated thus narrowing the lumen: *a, a*, endothelium and basement membrane; *b, b*, basement membrane ruptured by the ligature; *c*, exudate below the basement membrane; *d*, fibrin forming in the thrombus; *e*, red blood cells.



FIG. 251. Fibrin bundles extending from one wall of the vessel to the other; *a*, disintegrated round cells with leucocytes; *b*, fibrin bundles with interspersed round cells. The tissue at *a* becomes absorbed when the reaction ceases, that at *b* forms the permanent connective tissue without being replaced by fibroblasts.

healing in intestinal anastomosis. This process is attended by the exudation from beneath the cells of the homogeneous material which Waldeyer called "Kitt substance" which will hereafter be called by its English equivalent, "cement substance."

The collection of the platelets about the endothelium thus changed in form and the cement substance which exudes from beneath it forms fibrillar fibrin. The direct transformation of these fibrin fibrils into adult connective tissue heals the vessel. This change of fibrin into adult con-



FIG. 252. Network of fibrin bundles about more or less complete bundles: *a, a*, fibrin net-work; *b, b*, more direct bundles.

nective tissue is direct. The fibrin is not resorbed and replaced by the products of fibroblasts. This has been proven by my own researches and confirmed by Baitsell.

Fibrin bundles (Fig. 251) are formed only between two fixed points. When there are no fixed points the fibrin may form a network or the two may be combined (Fig. 252).

The nature of the cement substance above referred to cannot be stated in chemical terms other than that it reduces silver nitrate and because of its resemblance to silver chloride may be regarded as a chloride-containing substance. Since calcium is recognized as a necessary constituent of coagulation the cement substance may be hypothecated as a calcium chloride-containing substance.

It is interesting to note that this cement substance is abundant just beneath the vascular endothelium, and about the adventitia (Fig. 255), as

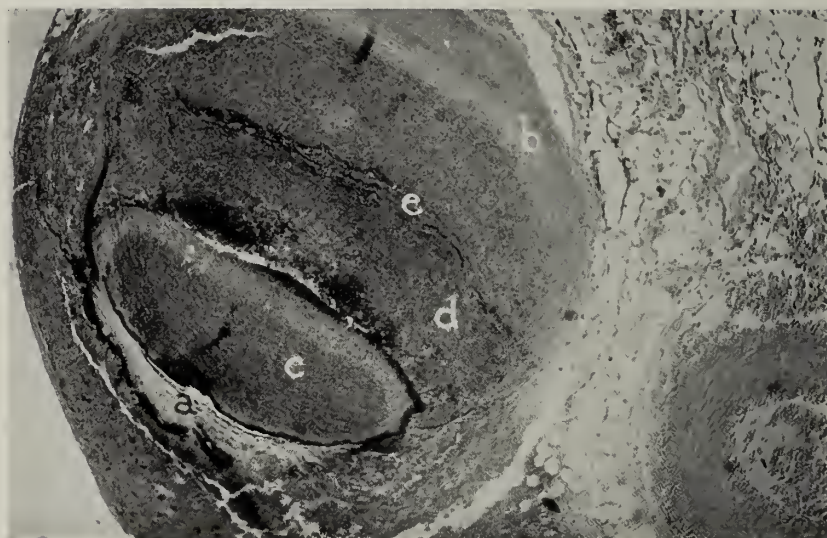


FIG. 253. Vein which has been painted with silver nitrate precipitating the cement substance: *a*, silvered part of vein; *b*, part not silvered; *c*, fluid blood; *d*, coagulated clot; *e*, columns of red cells. The failure of the clot to form over the silvered area is due to the precipitation of the cement substance by the silver.

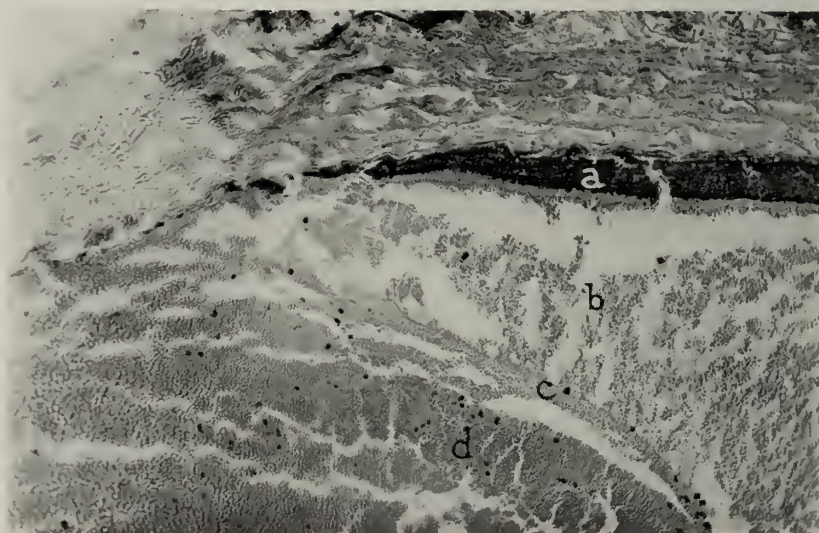


FIG. 254. Silvered vessel wall with fluid blood separated from a wall thrombus by a fibrin bundle; *a*, silvered wall; *b*, fluid blood; *c*, fibrin bundles separating this from *d*, a blood clot lying against the opposite wall. As in the preceding figure the blood does not coagulate when the silver has come in contact with the intima.

well as between muscle fibres. Surgeons have learned by practical experience that striated muscle is a good hemostatic. This is quite in harmony with the theory of Mills.

That thrombus formation is due primarily to the action of this cement substance is easily proven by painting one part of a ligated vein with silver nitrate. The action of the silver nitrate is to precipitate this substance and make it inactive. At the point where the silver has so acted thrombus formation does not take place (*a*, Fig. 253), while about

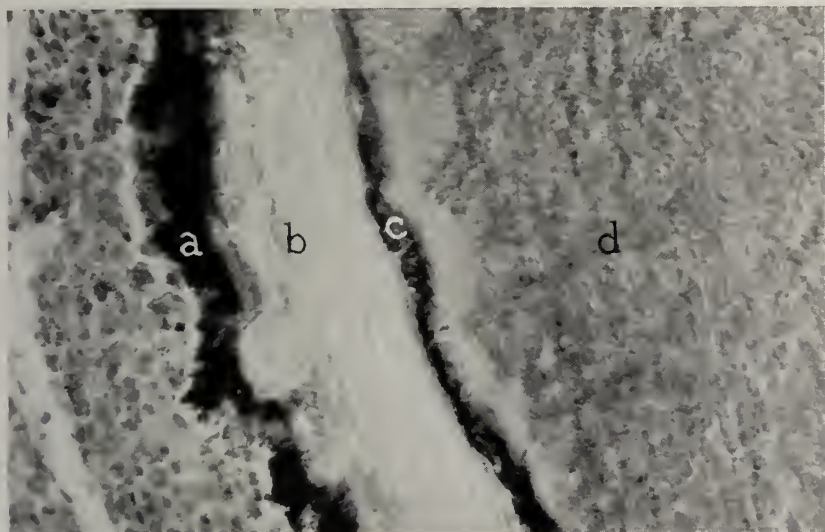


FIG. 255. Silvered vessel wall: *a*, adventitia; *b*, media; *c*, intima; *d*, post mortem clot.

the remainder of the vessel thrombus forms in the usual manner (*b*, Fig. 253). The blood may remain permanently fluid (Figs. 254 and 255) in part of the channel while the remainder is occluded by an organizing thrombus, just as is seen in phlebitis (Fig. 256). It is interesting to note in passing that the formation of adhesions in the peritoneum may be prevented by the same procedure.

Thrombi which form under these optimal conditions result in complete organization in a week or ten days. Forming thus they never escape their moorings and consequently postoperative embolism never results. Their formation requires a normal vessel wall, and maintenance of normal conditions for healing after ligation (Fig. 251).

Thrombus Healing by Second Intention. When the ideal healing set forth above is disturbed the process is different. Instead of a fibrillar fibrin being formed a granular one develops. The granular fibrin must

be replaced by fibres the result of cell action (Fig. 256). The attachment of the clot to the vessel wall therefore occurs only after these secondary factors become operative. A number of days are required for healing by this process. This is the method of wound healing according to the books. It is accomplished by the action of the fibroblasts. The important point here is that action of any force before the fibroblasts become operative may set the thrombus on its way and an embolus is the result.

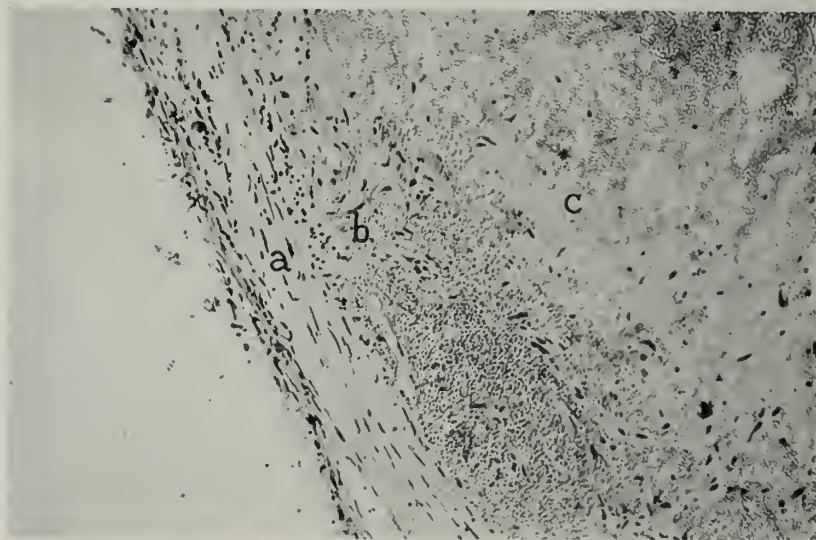


FIG. 256. Thrombus healing by second intention. The clot of granular fibrin is being replaced by fibrous tissue through the agency of the fibroblasts: *a*, vessel wall; *b*, fibroblasts forming new fibrous tissue; *c*, granular fibrin, etc. still to be organized.

In practical surgery this unfavorable result may follow two conditions: (1) The tissue may be inflamed at the time of operation. The vessel walls have been affected by the toxins or by the leucocytic infiltration which has destroyed the cement substance necessary to the formation of fibrillar fibrin. The fibrillar fibrin having formed is destroyed by the inflammatory process induced at the time of the operation, before sufficient time has elapsed to permit its transference into connective tissue. This is the least important of the two for usually by the time the infection reaches and penetrates the wall of any considerable vessel the process of thrombus organization has already proceeded to such a degree that dislodgment is not possible. (2) The tissues may be infected before the operation. Here the vessel wall is already in a state of reaction which has involved the cement substance, making it incapable of forming fibrillar fibrin.

When such a vessel is ligated an optimal clot cannot form. The granular fibrin is loosely attached and any stress may loosen it.

It cannot be too strongly emphasized that such clots are much more apt to be dislodged when the vessel ligated is large and when the distance to its tributary is short. The two sites where this is most likely to form are the cecal region where the veins soon join larger ones and particularly in the cystic vein which ends soon in the huge cava.

Therefore as a principle in surgery a vein in a state of reaction should not be ligated. If necessary to ligate under such conditions it should be made away from the site of reaction in normal tissue where the vessel is unaffected. About the cecum this can usually be accomplished, particularly when ligation of the omentum is necessary. In the cystic vein this is not possible for the inflammation in cholecystitis extends to the cava and a normal site for ligation cannot be reached. It is this fact that makes embolism relatively so frequent in cholecystectomies in inflamed gall bladders. The only prophylactic is to refuse to do ectomies in acute conditions.

Spontaneous Thrombosis. It is well to avoid stressing too strongly the relation of thrombus formation to the clotting of blood as already set forth. The essential factors in the coagulation of blood now generally accepted by physiologists is that there is a substance normally in the blood called prothrombin. Its conversion into thrombin is brought about by the action of thrombokinase and calcium. The thrombokinase is generally believed now to be supplied by the blood platelets and leucocytes in the presence of calcium. The above is correct for I copied it out of a book. Of these substances the only definitely known substance is calcium. The others might just as intelligibly be represented by algebraic symbols, x , y , and z .

A blood clot as generally conceived is a red semisolid gelatinous mass. It is essential to remember that a thrombus as chiefly concerns us here differs from the clot in that it is not red but greyish white and that the red cells are not an essential part of it. A red thrombus is a perversion of the purposive reparation action of nature in that the red cells hinder the repair the thrombus is designed to make. A red clot therefore indicates that there is something not quite right just as the presence of blood clot in a wound, while it may not prevent repair, does in a measure hinder its healing, and even a slight deviation from the normal chemistry of the blood may cause failure of the reparative process. Therefore the presence of a red plug in a vessel indicates a potential factor for mischief.

Because of these facts it is necessary to separate the various types of thrombi from each other though naturally transitions are common. It is

usual to recognize the white, red, leucocytic, purely fibrinous and the agglutinative. They may be considered in this order in conformity with generally accepted views.

The White Thrombus. The white thrombus is the ideal one. At least ideal thrombi are white. In elaboration of what was said about the action of the cement substance on the circulating blood it may be said that most likely it is the congregation of the platelets here that forms the clot. Other nucleated constituents of the blood likely take part. A preponderance of leucocytes, however, has another meaning. They come in response to irritation, dissolve rather than form fibrin and tend to loosen rather than to fix the thrombus.

Red Thrombus. In cases of thrombosis the greater part of the occluding column is red. It is said these have their beginning in a white clot which constitutes the head and the red part forms the tail. The red thrombus does not attach itself to the vessel wall. When examining such a clot, however, one is seldom able to make head nor tail out of it. Be this as it may, the red part augurs no good because it is unfavorable to healing of the vessel and the red part usually forms the embolus. A white clot may form the embolus but these are usually leucocytic in character and not cement substance platelet formations.

Leucocytic Thrombi. As a corollary to the white thrombi are the plugs made up only or chiefly of leucocytes. They occur about points of irritation as when an infective process approaches a vessel wall. These are most commonly found in smaller vessels about an area of infection. The increase in leucocytes in the dilated vessels about an inflammatory area may become so great that the vessels are occluded. If bacterial invasion has penetrated the vessel wall the leucocytes may temporarily restrain their entrance into the blood stream but they may lose their cohesion to the vessel wall, and together with the bacteria may float away into the blood stream and an infected thrombus is on its way. A leucocytic thrombus means therefore a combat with infection or dead tissue just as the same process in interstitial tissue spaces, but they are not to be confused with the white thrombus, nature's ideal process in vessel repair.

Hyaline Thrombi. These are produced by the decolorization of red thrombi. They are usually yellowish rather than white. They are of no interest to the surgeon for they represent intense reactive processes paralleling hemorrhagic infarctions.

Causes of Thrombi Not Due to Wounds. If the surgeon had to do only with thrombi due to wounds of his own making or those due to

accident our discussion might well end here. Unfortunately surgeons are frequently confronted by conditions in which vessels become occluded at a distance from wounds of their own making or wholly independent of any wound.

The first opinion worthy of serious consideration, advanced by Hunter, was that thrombosis was closely associated with changes in the vessel walls. Master surgeon that he was he saw this relationship more clearly than any one before or since. On the other hand, Virchow, master pathologist, saw the end stage in the autopsy room and therefore advanced entirely different theories of the origin of thrombi. One might as well try to compare the findings of a student of aseptic wound healing and one who studied only suppurative wounds as to harmonize the views of Hunter and Virchow.

The discussions as to the relative importance of the various factors may well be considered under three heads: 1, changes in the blood vessels; 2, changes in the circulation; and 3, changes in the blood itself.

1. **Changes in the Blood Vessels.** We have already discussed the influence of injury, operative and accidental, and inflammation of the vessel wall on the formation of thrombi and it is necessary now to discuss the changes incident to other processes.

Aschoff and particularly Lubarsch decry the influence of changes in the vessel walls. The latter presents the following thesis against the changes in the vessel wall as the initial process: *First:* A substance capable of preventing coagulation has never been demonstrated in endothelial cells. *Second:* Animal experimentation and observation on human material has not demonstrated a convincing relation between the loss of endothelial cells and coagulation. *Third:* Frequently, chiefly in the larger arteries, there are large defects in the endothelial cells and even marked unevenness of surface without the production of thrombi or at most only veil-like, hyaline network or granular exudates.

Despite such eminent authority I propose to set forth the results of my own experimental researches confirmed by abundant clinical experience:

1. It has never been contended that the endothelial cells possessed any coagulation-inhibiting substance. The function of the endothelial cells is to prevent the cement substance lying beneath them from coming into contact with the blood stream.

2. There certainly is abundant evidence that the loss of endothelium is followed promptly by coagulation of the blood. Everyone who has made attempts to secure blood vessel anastomosis has found this out. The action of endothelium of the blood vessels is altogether like that of

the endothelium of the peritoneum where it is known that adhesions occur when, and then only, the endothelium is destroyed.

3. In arteriosclerosis with atheromatous degeneration it is to be expected that thrombosis would not occur for the very obvious reason that the cement substance lying beneath the endothelium has been destroyed in the process of calcareous degeneration.

As has already been noted a destruction of the endothelial and sub-endothelial cement substance by means of silver nitrate tends to prevent

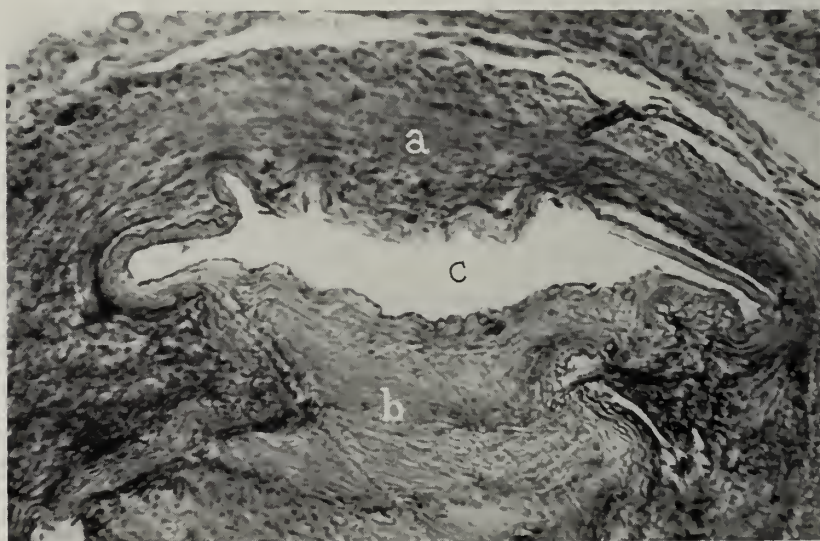


FIG. 257. Partial organization of the clot with retraction from the opposite wall: *a*, vessel wall; *b*, clot; *c*, partially restored lumen. In such cases the restored lumen may reach the dimensions of a normal vein.

coagulation. The surgeon may appreciate this better by comparing the formation of peritoneal adhesions. When the endothelium is irritated to the extent that the subendothelial fluids (the cement substance) come into contact with other peritoneal surfaces adhesions form. Likewise when the cement substance comes in contact with the blood stream thrombosis is the result. Aseptic injury to the endothelium is the most potent factor in producing a thrombus, just as it is in the production of adhesions. This is best illustrated in the ligation of vessels. A clot quickly forms if the endothelium is destroyed and in a week the clot is organized into connective tissue. If the endothelium is preserved a column of blood may be kept in a fluid state for a long time. I once maintained a fluid blood in the jugular vein of a dog three weeks.

Inflammation which approaches the vessel from without is potent for thrombus formation according to the character of the infection. The lesser infections produce a firm red clot capable of organization. The severer infections produce a white (leucocyte) or a gelatinous red clot not capable of rapid organization and in consequence liable to become loosened and produce the dreaded embolus.

In order to fully appreciate the effect of environment on clot organization one must needs go back to the preaseptic period of surgery. Ligation was followed in many instances by secondary hemorrhage. This simply meant that a thrombus capable of organization, due to infection of the wound, was not formed in the vessel proximal to the ligature and when the ligature separated, as a result of the necrosis of the vessel wall at the point of ligation, the thrombic plug became dislodged and hemorrhage followed. In postoperative embolism the same factors are operative but instead of the loosened clot blowing out, as it were, resulting in secondary hemorrhage it floats free in the blood stream and sets forth on its devastating mission. We still encounter this difficulty when operating in regions where infections are inevitable, as about the mouth and rectum and after the separation of the eschar following the use of the cautery.

2. **Changes in the Circulation.** The importance of changes in the circulation received much attention from pathologists during the periods when they were employed chiefly in the study of dead house pathology. In this material the changes in the circulation was the dominant factor. Most patients coming to autopsy have failure of circulation or they would not be there. To the surgeon this is of relatively little importance for the dead house is just the scene he hopes to avoid and he is little disposed to exercise his art on the class of patients whose circulatory apparatus is such as to invite the slowly developing thrombus. But the surgeon must remember that the changes in the blood stream are influenced not only by the disease for which the surgeon operated, but also by events incident to the operation, notably by the anesthetic and the duration of the operation itself; to these may be added, perhaps hemorrhage, and wound reaction or actual infection. It behooves the surgeon, therefore, to avoid as many as possible of the factors which tend to disturb the blood flow. Limitation of activity, posture, radical changes of food intake, and the like, also powerfully influence the dynamics of the circulation. It is the influence of these factors that should excite the interest of the surgeon and cause him to lend a ready ear to the discussions of those versed in the normal and abnormal circulation.

Much has been made of local factors in the circulation. It is believed that when a lumen of a vessel enters a wider space producing a whirling

motion that here is apt to be the site of blood coagulation. The same is true when there are sacculations of the vessel walls due to anomalies or previous diseases. This may be the condition which leads to the formation of thrombosis in the femoral veins in otherwise simple operations. This is often cited in cases of thrombosis in varicosities. Here often the changes in the vessel walls previous to the thrombosis, or a secondary injury, is ignored. These factors were much played up by the older pathologists. While it may have an influence on the site of a thrombus it can have but little on its actual development, for the patient is possessed of many of the same anatomic arrangements from birth to date and cannot in themselves exert any great influence. As a matter of fact such sites are not those that concern the surgeon, however much they may determine the location of terminal thrombi. Narrowing of a vessel from previous thrombosis or from compression from without no doubt plays a part, but here, too, often the inflammatory element producing the compression is ignored.

3. **Changes in the Blood.** Changes in the constituent elements of the blood may follow as a secondary factor any of the processes already discussed but coagulation is influenced by changes in the constituent elements of the blood quite independent of any other factor.

Blood Platelets. The influence of platelets on coagulation have been much discussed by pathologists. They assume the attitude that the platelets are mischievous little devils going about to see where they can congregate into a thrombus. As a matter of fact the platelets bear the same relation to thrombosis that leucocytes bear to inflammation: They do their best to repair impending damage. That they so often fail does not alter the fundamental facts.

Changes in the Red Cells. It is generally accepted that the coagulability of the blood is increased in acute hemorrhages. Whether this is due to an in-flow of thrombokinas from the tissues, as von der Velden would have it, is uncertain, but it is a pretty theory and should be allowed to stand for the benefit of those who insist on an explanation. The word sounds impressive and it may be the physiological equivalent of the anatomic term cement substance. Whether true or not, chronic anemias are not attended by an increased tendency to coagulation unless there is an associated weakening of the circulation.

Changes in the Leucocytes. That there is a tendency to increased thrombosis in leukemia may be admitted, but as de la Camp points out, the large liver, splenic changes and displaced diaphragm may account for this. With this is often associated the decrease in the heart beat. In

increase in the leucocytes, the result of infection, the dominant factor of course is the infection. It has not been demonstrated that the leucopenia has any influence on thrombosis.

Anomalies of the Blood-Plasma. It has long been known that the calcium content of the blood plays a determining part in the formation of thrombi. Surgeons commonly administer calcium salts to patients in whom the coagulation time is lengthened, thus paying tribute to the importance of calcium in forming thrombi. On the other hand, other elements hinder or prevent coagulation. Among those familiar laboratory substances which prevent blood coagulation are leech extract, peptones, pancreatic extract, and the like. Clinically, infections, primary diseases of the blood, biliary salts and the like play an important rôle.

POSTOPERATIVE THROMBO-EMBOLISM

The formation of a blood clot somewhere outside of the central circulatory system and its transport to a central vessel, usually the pulmonary artery, forms the supreme surgical disaster. In the lesser forms but a minor vessel may be occluded and a pleuro-pulmonary complication may arise the exact nature of which may be problematic. Embolism may therefore be divided into two general groups as Capelli does; the larger, usually terminal emboli and the smaller leading to pleuro-pulmonary complications.

Terminal Emboli. The larger emboli usually cause instant death; "like lightning out of a clear sky" is no exaggeration. The area occluded is usually sufficient to account for the rapid fatal termination. Schumacher calls it a "shock-death." In most cases, however, shock need not be assumed since the area occluded is sufficient to account for the fatal termination.

Death does not always follow the first embolism. Hours, days, even weeks may intervene between the first embolism, characterized by pain in the chest, dyspnea and bloody sputum, and the final fatal termination.

The emboli may be multiple. When single it is stated that it occurs on the right side though in three of my cases the left side alone was affected. When multiple, they are usually smaller and may be divided between the two sides of the chest.

Pathology. In the larger emboli there may be no changes in the lung, just a clot in one of the large pulmonary vessels—and that is all.

In those cases in which life extends for some time there are a great variety of changes. Secondary clots may extend throughout the vessels and there is a general infarction (Fig. 258). In the smaller ones the



FIG. 258. Terminal embolism of the lung. The center of the figure shows a number of occluded vessels. There is considerable edema of the lining surrounding these.

infarcted areas are pyramidal with the base to the pleura. If time sufficient elapses these may lose some of their deep red color because of resorption of the infarcted blood by the surrounding circulation. Escape of blood in these border vessels accounts for the blood sputum often observed soon after the accident. The pleural surface at the base of the

infarction pyramid is covered with an exudate, the cause of the pleural pain.

The minor degrees of embolism leading to recovery we can conceive of as undergoing organization of the infarcted area. How many of the



FIG. 259. Gangrene of the toes in chronic endocarditis. There was at first a blanching and gradually a darkening of the skin of the toes without attending pain.

so-called postoperative pneumonias cannot be estimated. They can only be suspected from the time and nature of their onset and the character of the physical signs, the chief of which is the absence of tubular breathing.

Histology. From the foregoing it is obvious that the microscopical anatomy may vary between nothing at all, simple edema, fresh infarct of wide scope, the disintegration of the infarcted blood, even early stages of organization. There is nothing specific and the gross anatomy tells it all.

Arterial Embolism. Arterial emboli most commonly arise from the valves of the heart. Therefore the end results only concern the surgeon. The result depends on the size of the floating object. An entire organ, an extremity or only small areas may be affected.



FIG. 269. Gangrene of the foot from embolism in endocarditis. Following excruciating pain in the foot total gangrene followed.

Pathogenesis. We are concerned here only with embolism of the extremities. Those involving the internal organs will be considered in the proper place. With the escape of a clot a vessel of some size is occluded. If the vessel is small only small areas may be involved and the onset unheralded or at most the pain is slight (Fig. 259). When a larger vessel is shut off the pain is excruciating. This is followed by the blanching and the cooling of the affected part and then often by gangrene (Fig. 260).

Pathology. The affected parts are cold at first and tend to become dry if the area affected be not large. Otherwise the tissue may soften as a moist gangrene. The section of such area lacks the infiltration by blood commonly seen when the gangrene is due to obstruction of the venous circulation. The offending body is not easily discovered and is commonly in larger vessels than one would expect from the extent of the gangrene; this is true if the possibility of prompt development of the collateral circulation is not kept in mind.

Histology. There are little changes. Death of tissue without cellular activity is the classical finding. Anything more must be due to the attempts at establishment of collateral circulation.

Literature

Thrombosis and Embolism. The first expression on the subject of interest to the surgeon, was made by Hunter (Trans. of Soc. for Improv. of Med. and Chir. Knowledge, 1793, i). He ascribed to inflammation of the veins the fundamental factor in thrombosis and compared intravascular coagulation with fibrinous inflammations on serous surfaces. A more apt comparison has never been made since. Cruveilhier (Anat. path. de corps human, 1829-1842, i and ii) also linked thrombosis with inflammation of the veins. Rokitsansky (Lehrbuch d. path. Anat., 1844, i and ii) emphasized the importance of primary changes in the blood due to general conditions and Virchow (Handb. d. spec. Path. u. Therapie, 1854, i; Gesammelte Abhandlungen, 1856) developed the conception to the scope now generally accepted and in fact, was the first to use the term "thrombosis." He admitted the influence of inflammation of the veins and the changed conditions in the blood but he emphasized the mechanical factors in the circulation as the principal factor. The local conditions were ignored and the general conditions were emphasized. We see thus early the divergent new points held by Hunter the surgeon and Virchow the pathologist.

The first attempt at differentiation between thrombi and coagulation was made by Mantegazza (Gazz. med. Lombard, 1869) and Zahn (Virchow's Arch., 1875, lxii; Virchow's Arch., 1884, xcvi; *ibid.*, 1885, cii). They studied thrombi composed of leucocytes and granular material without the presence of any fibrin. This divided sharply the "white thrombi" from coagulation. This showed for the first time that thrombi do not necessarily contain all the elements of the blood. Von Recklinghausen (Handb. d. allg. Path. d. Kreislauf. u. d. Ernährung, Deutsch. Chir., Lief. 2, 3, 1883; Deutsche Arch. f. klin. Med., 1885, xxxvii) emphasized the influence the mechanism of the circulation plays in the formation of thrombi of this class. According to him it was the incident slowing of the circulation which allowed the white corpuscles to assume a peripheral position in the vessels.

A granular material had been noted as a constituent of some thrombi. Bizzozero (Virchow's Arch., 1882, xc) associated these with the "elementary bodies," first described by Zimmerman (Virchow's Arch., 1860, xviii). He was the first to designate them "blood platelets." Since that time the blood platelets have played a large part in the formation of thrombi. The origin of the platelets has given rise to much discussion not yet ended. As indicated by the name he gave them Zimmerman regarded them as immature red blood cells, while Wright (Jour. of Phys., 1891, xii; Virchow's Arch., 1906, clxxvi; Boston med. and surg. journ., 1906, June, Nr. 23) regards them as the product of the megakaryocytes of the bone marrow. More recently Ogates (Ziegler's Beitr., 1912, lii, i), Aschoff (Ziegler's Beitr., 1912, lii, 2) and Schridde (Zentrbl. f. Path., 1911, xxii, 20) have come to the same conclusion.

Fibrin in clots was from now on regarded as an accidental admixture. This banishing of fibrin from consideration as an important element in thrombi was due to the discovery that in some thrombi it was absent or present only in small amounts. More recently there has been a revival of the interest in the local origin of thrombi, first fostered by Baumgarten (Die sogenannte Organization d. Thrombus, Leipzig, 1877; Virchow's Arch., 1879, lxxviii; Verhdlg. d. D. Path. Gesell., 1902, v), Dietrich (Verhandl. d. D. path. Gesellsch., Jena, 1912, xv, 372); Cornil (Presse Med., Paris, 1897, ii, 102; Bull. spec. anat., 10. Dec. 1884), Widal (These de Paris, 1889) and others.

The evidence of history permits the summary that there is a thrombosis due to local conditions and one due primarily to general conditions.

In the presentation of this chapter it has been my object to emphasize the purely surgical aspects. In so doing it has seemed necessary to stress the local causes of thrombosis from which the dreaded postoperative embolism is derived. Since there are no specific prophylactic measures the surgeon's only means of prevention is to avoid operation when possible on certain types of individuals and to employ a technic which avoids injury to vessels incapable of producing prompt healing of the vessel.

The literature here cited will lead the student into broader paths, particularly to those studies in which fatal embolism follows conditions not operative in origin, which begin as a phlebitis of small vessels, which gradually extend into and occlude large vessels, which may kill without any part of a thrombus having become detached. These are conditions which are revealed chiefly in the autopsy room. Since these sometimes follow operations the surgeon has more than a general interest in their occurrence.

A few fundamental papers may be cited. As a general study none equals Welch's (*Allbutt's Syst. Med.*, Macmillan Co., London, 1899, vii, 155) classical presentation. The importance of stagnation was emphasized by Eberth and Schimmelbusch (*Fortschr. d. Med.*, 1885, iii, p. 379; 1886, iv; 1888, vi; *Virchow's Arch.*, 1886, ciii, 1887, cviii). They emphasize the difference between thrombus formation and coagulation. Welch (*Trans. Path. Soc. of Phila.*, 1885-87, xiii, 281-300) opposes their opinion.

Osler (*Brit. med. Jour.*, 1886, i, 917) emphasizes the importance of the platelets. He states that the superficial part of a white clot is comprised of blood platelets. In the deeper parts the blood platelets are found disintegrated. The colorless corpuscles play an altogether insignificant part. This observation is of fundamental interest to the surgeon. This, together with Mills' more recent work may well form the basis for future study in so far as the problem relates to the practice of surgery. The chief interest in Mills' (*Am. Jour. Med. Sc.*, 1926, 4, 172) paper in this connection lies in the fact that the most active coagulating substance is found where silver nitrate shows the cement substance to be most abundant. Hence here his studies and mine come together.

It is particularly desirable that the surgeon free himself from the theory that the leucocytes are other than undesirable elements in friendly thrombus formation. Zenker (*Zeigler's Beitr.*, 1895, 27, 448) combats the notion that there is any connection between destruction of white corpuscles and the formation of fibrin. The coagulation starts from masses of plaques and detached vascular endothelium. These latter produce the fibrin ferment. He overlooks the presence of the cement substance. Without this the endothelial cells are powerless to act. Fisher, Wassel and Tannenberg (*Deutsch. med. Woch.*, 1929, 55, 524) believe that thromboses due to vascular change and those due to changes in the blood stream are not identical. The majority, they believe belong to the last named group, particularly the septic thromboses which begin at some distance from the large vessels. The altered blood coagulates wherever the circulation is slowed. These authors have presented a noteworthy contribution. Certain cases of thrombosis after appendicitis, particularly those not operated on, and in sinus thromboses, following hair follicle infection about the nose, would seem to belong to this class. These authors emphasize the difference between thrombi developing at the site of injury and those beginning in small vessels as a result of infection, at a distance from the great trunks. These are due to modification of the blood and alterations in the dynamics of the circulation. Aschoff (*Virchow's Arch.*, 1892, cxxx, 93-145) regards the presence of the blood platelets together with changes in the vessel wall as the essential features, without however pointing out that it is the changes in the vessel wall which account for the accumulation of the platelets.

The literature on the clinical phases of thrombosis and embolism is endless. That dealing with postoperative embolism will be emphasized here. It is mostly casuistic and mostly ends nowhere and it is of interest chiefly because it indicates that all surgeons alike have their problems.

Kuhn (*Mit. a. d. Grenz. d. med. u. chir.*, 1929, 41, 329-388) finds that embolism is particularly an accident of advanced years, being most frequent between 51 and 60 years. This is true of medical rather than surgical cases. The percentage is much

increased in the corpulent in both medical and surgical patients. Calmann (*Zentrbl. f. Gynak.*, 1928, 52, 2346) thinks there is a hereditary disposition to embolism. It is much more common after abdominal operations, particularly after operations on the adnexa and in myomectomies. Bland-Sutton (*Lancet*, 1909, i, 147-152) thinks the chief cause of thrombosis and embolism is sepsis. Fränkel (*Arch. f. klin. Chir.*, Berl., 1908, 86, 531-545; also *Verhandl. Deut. Gesell. f. Chir.*, 1908, 27, pt. 2, 6-30) finds embolism in 5% of laparotomies, half of which are accompanied by embolism. He believes those at a distance are likewise caused by infection. Zurhelle (*Verhandl. Gesell. Deut. Natur. u. Aerzte.*, 1907, Leipzig; 1908, pt. 2, 174, 177) in 3500 gynecological operations had 19 cases of pulmonary embolism with 15 deaths. The most common age was from 36 to 55 and may come on any time between the fifth and thirty-eighth postoperative day. It is most common after myoma operation. Embolism most commonly follows after thrombosis of the pelvic veins, never after thrombosis in the saphenous. Klein (*Monatschr. f. Geburt. u. Gynec.*, Berlin, 1911, 34, 549) in 5524 operations had 40 thromboses and emboli; 11 fatal embolisms in 15 cases. Stohr and Kazda (*Deutsch. Ztschr. f. Chir.*, 1928, 208, 105) found that in 20,000 autopsies there were 134 cases of postoperative embolus. Sulger and Bozzin (*Deutsch. Ztschr. f. Chir.*, 1929, 216, 175) studied the blood in 60 operative cases before and after operation. The bleeding and coagulation time was not altered. The platelets were increased in a few cases. Detering (*Beitr. z. klin. Chir.*, 1928, 144, 416), reporting on about 25,000 cases found thromboses in 2.4% in 1919, which was raised to 16% in 1927. Embolism occurred in 3.4%. Post-operative embolisms are very much more apt to follow postoperative than preoperative thromboses. Rippel (*Wien klin. Wchn.*, 1928, 41, 594) notes the increase of the proportion of fatal embolisms as compared with like statistics in 1913. In 9 cases there was no visible thrombophlebitis. Obviously the clot escaped leaving no trace at the point of origin. It is interesting to speculate as to whether or not the state of nutrition may have had some effect. There seems to have been a marked increase in all hospitals since before the war; likewise there seems also to be an increase in Switzerland according to de Quervain (*Schweiz. med. Wchn. Basel*, 1925, 45, 497).

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